Drug Utilization Review Board
October 17, 2018

Lisa Chew: Good morning everyone. We are going to convene the Washington State Drug Utilization Review Board. I want to remind everyone that this is a recorded meeting so please be sure to state your name before making comments. Let's start off with introductions. Let's start at this end of the table.

Jennifer Brown: Jennifer Brown, pharmacist program manager at Amerigroup Washington.

Kerrie Fowler: Kerrie Fowler, senior pharmacy director for Coordinated Care in Washington.

Petra Eichelsdoerfer: Petra Eichelsdoerfer, pharmacy program manager for Washington United Healthcare.

Diane Schwilke: Diane Schwilke, committee member.

Virginia Buccola: Virginia Buccola, committee member.

Nancy Lee: Nancy Lee, committee member.

Alex Park: Alex Park, committee member.

Dale Sanderson: Dale Sanderson, committee member.

Lisa Chew: Lisa Chew, committee member.

Jordan Storhaug: Jordan Storhaug, committee member.

Catherine Brown: Catherine Brown, 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.

Ryan Pistoresi: Ryan Pistoresi, Health Care Authority.

Emily Peltier: Emily Peltier, Health Care Authority.

Judy Zerzan: Judy Zerzan, I am the new chief medical officer at the Health Care Authority. I came from Colorado. I was chief medical officer for the Medicaid program there a little over nine years and I'm originally from the Northwest so I am excited to be back and pharmacy is one of the things I like a lot and so I was able to fit this in and I'm excited to meet you all and work with you. Thanks.

Leta Evaskus: And on the phone.

Rick Pope: Good morning. My name is Rick Pope. I'm a pharmacy account manager with Magellan Health.

Lisa Chew: Thank you.

Jose Zarate: Jose Zarate, Health Care Authority.

Donna Sullivan: That should be all.

Lisa Chew: All right. Welcome, Judy. All right. Let's go ahead and get started on our first agenda item. Richard, are you ready? Your slides are up for the dermatologics.

Richard Pope: All right. Thank you. Good morning everyone. If we go through the slides they are going to be arranged as… in a manner so that we will first talk about the disease overview and then we will talk about indications, the dosage forms and formulations, and any guideline updates. As the slides should indicate slide 3 now, this is the botulinum toxins. First I want to make note of the fact that when we start these presentations and you see the slides for each class you will see a couple of different titles on there. The first is representative of the nomenclature and the

grouping that we use at Magellan. The second is the Apple Health. They are the same class, the same drugs, but sometimes they may have different names, but we're mentioning both just for completeness sake.

On slide 4 you will see an overview of the disease states for the botulinum toxins. Here we're going to be talking about the non-cosmetic use of the agents in this class. One of the primary uses is cervical dystonia. Previously it was known as spasmodic torticollis, a painful localized neurologic movement disorder. Symptoms were caused… the intermittent [inaudible] sustained contractions of the neck to control the position of the head. The head position is altered and the effect can spread down to the shoulders. Another common treatment for this disorder is muscle spasticity, eyelid twitching, blepharospasm, improper eye alignment, strabismus and axillary hyperhidrosis. Next slide, please.

Here you're going to see a listing of the indications for the four main medications in this class—Dysport, Xeomin, Botox and Myobloc. All indications are all specific to the location of the spasticity. The general order of the slides going through this presentation is going to be alphabetical. So they are not listed in any other manner of importance. They are listed alphabetically. There is no generic available or biosimilar available for this group. The general mechanism of action for most of these is to inhibit the release of the citicoline from the peripheral or cholinergic nerve ending. This occurs… the binding of toxins to specific surface receptors on the nerve ending. The toxins enter the nerve terminals and cause inner-cellular blockage of the neurotransmitter activity. Next slide.

Next we see the various dosing and availabilities for each medication and the respective indications. All four medications are found in unit dose vials. The doses may be repeated when the clinical effects from the previous administration begins to diminish. In general, repeated doses should not be done more frequently than every three months. Medications in this class do carry a boxed warning regarding the potential for [inaudible] spread of the toxin effect. Although the effects are generally localized and the drug is generally not detected in the blood the effects can sometimes be observed beyond the site of the location. Some of the symptoms could manifest themselves as asthenia,

generalized muscle weakness, double vision or general blurred vision. In terms of patients who are patient these are also pregnancy category C in the old nomenclature, which was there is insufficient testing and insufficient clinical evidence to say it is specifically safe and of course then you do a risk benefit assessment when they are being used. Next slide.

Here we have the two remaining meds with their specific indications. Again, availability is in unit dose vials. In terms of pediatric applications Dysport is approved for the treatment of lower limb spasticity for patients at least two years of age. Safety and efficacy has not been established in kids for this product for any other indications. Botox has various pediatric safety indications for blepharospasm and [inaudible]. The patients must be at least 12 years of age. Cervical dystonia, but they must be at least 16 years of age. Urinary incontinence due to neurogenic [inaudible] activity or over-active bladder in patients that have to be at least 18 years of age and for spasticity axillary hyperhidrosis and chronic migraine prophylaxis. Again, they must be 18 years of age. Safety and efficacy of Xeomin and Myobloc in children has not been established. Next slide, please.

Some guidelines from the American Academy of Neurology you'll see guidelines listed here. In 2016 they updated their guidelines that you'll see listed for these four specific indications or diagnoses for blepharospasm, cervical dystonia, adult spasticity and headache. Next slide, please.

Looking at previous guidelines from 2008 the four that we just looked at were updated, as I said. These others have not been updated since the initial 2008 American Academy of Neurology guidelines. They are still in effect and still good. This involves spasticity, movement disorders and autonomic disorders and pain. You'll see on the second bullet point Botox and Myobloc were available at the time of this 2008, others were not. For these indications that we have listed here on the 2008 guidelines there is an update in progress, but no published time that it will be released. Next slide.

I will stop and pause and after going through the first step any questions? Am I going too fast or going too slow?

Lisa Chew: Richard, you are going perfect. Any questions for Richard?

Richard Pope: We'll press on. We are now on slide 10.

Leta Evaskus: Richard, hang on. We are going to do the policy part.

Richard Pope: I'm sorry. I have my agenda here. My apologies.

Lisa Chew: Should we do stakeholders first?

Leta Evaskus: No. You do your policy first and then the motion.

Lisa Chew: Okay.

April Phillips: So the botulinum toxins are spread across two therapeutic classes. There's the dermatologic, the agents for wrinkles, lipoatrophy, and other aesthetic uses. This is not going to be an Apple Health PDL class because it is considered cosmetic and the only product in that class is the Botox cosmetic. So the other class is the neuromuscular blocking agents, neurotoxins with Botox, Dysport, Myobloc and Xeomin. So currently that class will not be implemented as an Apple Health PDL at this time. There is an HTA policy and Ryan will present that.

Ryan Pistoresi: Good morning. There was an HTCC decision. So the Health Technology Clinical Committee who reviewed Botox for the use in chronic migraine and chronic tension-type headaches. The decision was made back in 2017, but was recently updated on July 13, 2018. I'm going to read the coverage determination. So for the treatment of chronic migraine with onabotulinumtoxinA is a covered benefit with conditions. For the treatment of chronic tension-type headache with onabotulinumtoxinA it is not a covered benefit and treatment of chronic migraine or chronic tension-type headache with acupuncture, massage, trigger point injections, transcranial magnetic stimulation or manipulation manual therapy is not a covered benefit. The HTCC reimbursement determination has a limitation of coverage for the onabotulinumtoxinA

for treatment of chronic migraine and that it is covered when all of the following criteria are met. That the patient has not responded to at least three prior pharmacologic prophylactic therapies from two different classes of drugs and that the condition is appropriately managed for medication over use and onabotulinum injections must be discontinued when the condition has shown inadequate response to treatment defined as less than a 50% reduction in headache days per month after two treatment cycles and that there is a maximum benefit of five treatment cycles. Additional treatment cycles may be considered at agency discretion. And that is available at our HCA website under the HTCC program.

Donna Sullivan: So with the Health Technology Assessment Committee and program is different from the Pharmacy and Therapeutics Committee, but their decisions are binding by statute. So we just wanted to let you know that that is the policy for the migraine headaches and there is nothing that this committee can do to change that particular policy at this time. So I just wanted to make that clear to everyone that that is the policy that was approved by the HTCC and that we are legally obligated to follow.

April Phillips: So for our recommendation would be to continue the current policy.

Leta Evaskus: We can do stakeholders now.

Lisa Chew: We have one stakeholder, Dr. Jill Kerrick Walker. If you could come up to the podium.

Jill Kerrick Walker: I'm with Ipsen Biopharm and don't have anything to add. So I'll respectfully give my time up.

Lisa Chew: Okay. Thank you very much. Any questions from the committee members for April or Donna or Ryan? So we have a motion here if someone feels comfortable making the motion for the topic on slide 11.

Amber Figueroa: I'm sorry for a late entry. Was its use addressed for cerebral palsy?

Donna Sullivan: We are not going to put this class on the preferred drug list. So for any indication that is FDA approved the plans will, you know, treat those cases on a case-by-case basis for medical necessity to the FDA label.

Diane Schwilke: I move that the Apple Health Medicaid Program implement the limitations for the Neuromuscular Blocking Agents – Neurotoxins drug class listed on slide 11 as recommended.

Dale Sanderson: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? Then the motion carries. All right, Richard. We are on to the next topic, hematologic agents.

Richard Pope: Thank you. Hematologic agents are the hemophilia agents. That is what we are going to look at. Hemophilia is an umbrella term that encompasses a number of different diseases, but generally refers to a couple of specific instances and you'll see what I mean as we go along. It is a rare inherited bleeding disorder where the blood does not clot properly due to an absence of one or more coagulation factors present in normal blood. It is identified as an X-linked congenital bleeding disorder. The frequency generally is about 1 in 5,000 to 10,000 births. It typically affects males due to the X-linked inheritance, but females can be affected although they generally are carriers. About 30% of newly diagnosed cases occur with no prior family history and attributed to spontaneous mutations or deep hidden carriers. The mutation is going to be in the Factor VIII Factor IX gene. The World Federation of Hemophilia estimates the global rate is about 400,000 people affected. In the United States it is generally put between 17,000 and 20,000 persons. There are two main types of hemophilia as I indicated—Type A and Type B. Type A is Factor VIII deficiency or classic hemophilia. It's far more common and runs anywhere from about 80 to 85% of all hemophilia patients. Here they exhibit low or missing levels of Factor VIII clotting factor and then they are stratified as far as the reduction in their endogenous clotting factor whether they are mild, moderate or severe hemophiliacs. Similarly for

Type B, also known as Factor IX deficiency or Christmas disease. In case you're wondering why it's called Christmas disease. It was discovered over the Christmas holiday in England years ago. That's how it came to have that name. Those with Type B also have lower missing clotting Factor IX. Next slide, please.

As I said it's an umbrella. So hemophilia can also refer to a number of other rare factor deficiencies. You'll see them listed here from Factor I, II, V, X, up to Factor XIII. These are far less common than your traditional hemophilia A or hemophilia B. This is best exemplified by Factor XIII which occurs in about 1 of 5 million births. Next slide, please.

Also we have von Willebrand disease, which is under the hemophilia umbrella and it is generally considered as a separate disease type. Here it is an inherited bleeding disorder related to the absence or defect in the von Willebrand Factor, which is a clotting protein needed to maintain hemostasis. Von Willebrand binds to Factor VIII and platelets to generate the plug during the clotting process. The prevalence of this disease is estimated anywhere between 1 to 100 to 10,000 individuals. Its gene equally in males and females. There are three major types of von Willebrand – Type 1, Type 2, Type 3 and it has to do with the deficiency of the von Willebrand factor. Type 1 accounts for about 75%. Type 2 is a little bit more severe in about 25% and the rarest is Type 3, which is a complete von Willebrand factor deficiency. Next slide.

Here you're going to see over the next six slides you're going to have the various medications and their indication. All of the products, again, listed alphabetically are stratified. Sometimes we'll look at the Factor 8 replacement products first and then we'll look at the Factor 9 replacement product and other factor replacement products. The first six meds we have here listed are Advate, Adynovate, Afstyla, Alphanate, Eloctate and Helixate. When I first started back in hemophilia years ago I was happy to note, and you will also note, that most of the convention of the naming of these products for Factor VIII deficiency has an 8 in there. It's not always the case anymore and for the Factor IX deficiency most of the products are going to have a 9 in there or you will see the Roman numeral IX somewhere in the name. Now as far as the mechanism of action it is very simple for these Factor VIII and Factor IX products are

given intravenously and they are designed to supplement the endogenous coagulation factor and bring it up to an acceptable level in the patient to be able to maintain a normal plotting process and stop bleeds. Next slide.

Here we have more Factor VIII products Hemofil, Humate, Koate, Kogenate, Kovaltry, Monoclate and Novoeight. I do want to make note that there was one product that just entered to the market and that is Jivi. Jivi is a pegylated Factor VIII from Bayer. It carries many of the same indications as the other products and, as I said, it just entered the market very recently. So unfortunately it was not able to be put in the slides here. It is a pegylated product. Probably the Bayer people will cringe, but it is a pegylated product very similar in use to Adynovate which was on the previous slide. Next slide, please.

The remaining Factor VIII products listed here Nuwiq, Obizur, Recombinate or Xyntha. Obizur, as you'll see, the second one down is the only one that is really indicated for acquired hemophilia. That is where not the genetic link [inaudible]. It is just a spontaneous… essentially an autoimmune disease that develops where they lose their Factor VIII and it's not necessarily a genetic passing on and that is the only one indicated. We also now are going to transition the bottom half of the slide to the Factor IX products. Here we start with AlphaNine, Alprolix and Bebulin. Next slide, please.

We continue with the Factor IX products BeneFIX, Idelvion, Ixinity, Mononine, Profilnine and Rixubis. You'll see a number of these are recombinant. Some are pooled plasma. They may be pegylated. The primary ones are the recombinant or the pooled plasma. Recombinant then also gets into particularly the Factor VIII gets into generation—third generation is one word. It has [inaudible] proteins to reduce any reaction or also has a reduction in potential of transmission of anything. Pooled plasma still is a very good and viable product. It is arguably by [inaudible] which is a medical and scientific advisory committee for the National Hemophilia Foundation. Provisionally it is given a little bit of an edge. Recombinant products are given a little bit of an edge over pooled products. However, there has not been a known viral transmission from a pooled product factor since 1999. Next slide, please.

Here we have the Factors VIIa and the activated prothromblin complex concentrate. These are… I hate to use the word specialized, but these are specialized products that are often employed in cases where a Factor VIII or Factor IX patient has development of inhibitors and they have a particularly high [inaudible] or [inaudible] and they need a bypassing agent. So these are commonly known as bypassing agents because they will continue the cascade to the clouding process whereas the inhibitors will just reduce the efficacy of straight Factor VIII or straight Factor IX. You will also see listed here Factor X and Factor XIII products. These again are for some of the very rare ones. The last group are the von Willebrand products, Vonvendi and Wilate. Next slide, please.

Here we have some of the various dosing for many of the products. Not all of them will have dosing and that is because the dosing with [inaudible] comes from the manufacturers and is recommended dosing in prophylactic therapy. There's two basic types of therapy when it comes to hemophilia. That's on-demand where you treat a bleed. Prophylaxis is the idea that you maintain an endogenous level of factor so that you are able to prevent bleeds. When you talk about bleeds you're talking particularly about those that are more moderate and severe hemophiliacs that are noted for… particularly the severe hemophiliacs are noted for having spontaneous bleeds for no reason or cause at all. Primarily these occur in joints, but they can occur in soft tissue areas. So the idea of prophylaxis is to reduce the annualized bleed rate for spontaneous bleeds. You will see the dosing listed here. If it has an N/A then that indicates that that product is primarily used only in on-demand situations. For the most part all the products in the hemophilia category are pregnancy C or they are the new nomenclature where there is insufficient evidence to make a determination of potential harm to the mother and again you defer to risk benefit. Next slide, please.

We continue with the dosing and availability. Again, all of these products are in single-dose vials and used… mixed only when necessary. Here for the first time we're going to talk about a specialized group in geriatric patients. Most clinical studies for [inaudible] products… well, the clinical studies for [inaudible] products are all open-label studies and most of them did not include a sufficient number of subjects 65 or older to make

a determination of… if there was any alteration of efficacy in older patients. Treatment should be individualized as it is in on-demand situations for every patient in hemophilia and those… some of the analysis is based on weight, severity and disease and other things. Next slide, please.

Here's the last group of Factor IX products and their dosing for prophylaxis. Next slide.

I'm sorry. Now we're on the last slide. As far as guidelines there are two bodies that product guidelines—the World Federation of Hemophilia updated theirs in 2014. They have a list of principles for care and treatment. The other primary one is the… as I mentioned earlier the medical and scientific advisory committee for the National Hemophilia Foundation they essentially product recommendations which are guidelines in hemophilia. They range from everything about factor storage and the amount of factor recommended for patients to be on hand to specific products that may have an issue or may not have an issue and general recommendations and treatments. Those are oftentimes the general recommendations and treatment for them and are updated annually. I think their latest one for 2018 is recommendation number 253. You'll see point three under the World Federation of Hemophilia teaching patients to recognize bleeding aura which is experienced as an outward bleed. I will take just a moment if you will allow when I have been fortunate enough to be a pharmacist at hemophilia camp it was really amazing to see kids as young as 7 that are taught to infuse their own factor and will come in after playing volleyball in the sandpit and say, "Hey, I know I've got a bleed going on." And they will just infuse themselves, ice it, wait about a half an hour and go back out and resume their activities. The last point under the World Federation of Hemophilia guidelines is an important one with hemophilia and maintaining good oral health. But it also refers to, and I'm going to spin upon that, that both the World Federation of Hemophilia and National Hemophilia Foundation also incurred hemophiliacs to be up and active and participate in those activities which are allowable considering their disease state and maintain a good healthy lifestyle. You'll also see their guidelines for von Willebrand's disease listed at the bottom. Next slide.

Madam Chairperson, it's back to you.

Lisa Chew: Thank you, Richard. Any questions?

Dale Sanderson: Center of Excellence required? What is Center of Excellence?

Richard Pope: I'm sorry.

April Phillips: I think this question is for me. This is April. The Center of Excellence is a federally-recognized hemophilia treatment center and is 340B eligible. We currently have two OHSU and Blood Works Northwest for Washington State.

Donna Sullivan: Yes, they are required to get their hemophilia factor from the Center of Excellence.

Lisa Chew: Any other questions? April, do you want to cover the…

April Phillips: The current limitations this particular therapeutic class the hematologic agents miscellaneous anti-hemophilic products is a therapeutic class that is carved out from the managed care. It is strictly a fee-for-service that we take care of. It is required the Center of Excellence or COE is required to get the factor. And then our recommendation is to continue that.

Donna Sullivan: Again, this is one of those classes that will not be put onto the preferred drug list and all of the… there is no preferred products in this class. They are all open access through the Center of Excellence as determined by the prescriber.

Lisa Chew: Any other questions?

Alex Park: So when we say Center of Excellence are we referring to the designated hemophilia treatment centers that the CDC lists out?

Donna Sullivan: When we say the Center of Excellence we're specifically calling out the Oregon Health Science University Hemophilia Treatment Center and Blood Works Northwest as the hemophilia treatment center.

Lisa Chew: We have four stakeholders. Ms. Shirley Quack, Dr. Jessica Charlet, Dr. Sharon Cahoon-Metzger and Ms. Stephanie Simpson. If you want to come up to the podium. Please state your name and who you represent and you will have three minutes for comments. Also committee members there's also a letter from the National Hemophilia Foundation in your packet.

Shirley Quack: Good morning members of the board. My name is Shirley Quack and I am the managed care liaison at Genentech. First I want to thank the state and the committee for putting together a comprehensive review of anti-hemophilic drugs as much as hemophilia A as a bleeding disorder that results in uncontrollable bleeds. So having a comprehensive list allows patient access to life-saving medication to manage their bleeds. Today I am here because I want to share with you updated information on a recently approved novel medication for hemophilia A patients. Hemlibra was FDA approved at the end of last year in 2017 to reduce the number of bleeding frequencies in patients with hemophilia A with inhibitors. It is a monoclonal antibody that mimics Factor VIII and so it is not a factor product. Two weeks ago Hemlibra was FDA approved for hemophilia A patients without inhibitors expanding and broadening the original indication. The Haven 3 study was a pivotal trial in patients without inhibitors. In this study patients who were treated with Hemlibra prophylaxis demonstrated statistically significant and clinically meaningful reduction in their annualized bleed rates. And additionally a higher proportion of patients who were treated with Hemlibra prophylaxis also reported zero bleeds compared to patients who did not receive prophylaxis. And the safety profile for Hemlibra is tolerable. This demonstrates Hemlibra's strong efficacy in preventing and also reducing the number of bleeding frequencies in patients who have hemophilia A with or without inhibitors and also in adults and pediatric patients. So thank you members of the board for this time to update you on the exciting information on Hemlibra. We're prepared to do an in-depth review of the clinical data for this new indication as requested. Thank you again for putting together a comprehensive list of anti-hemophilic drugs for patients with hemophilia A. Thank you.

Lisa Chew: Any questions? Thank you. Next is Dr. Jessica Charlet.

Jessica Charlet: Hello. I'm Jessica Charlet. I'm the medical science liaison with Bayer on the West Coast. Today I'm presenting you our new product that has been approved by the FDA on August 29th this year. Jivi is a [inaudible] Factor VIII variant that is site specific [inaudible] with a single 60 [inaudible]. Jivi is a third generation recombinant [inaudible] product indicated for use in previously-treated hemophilia A patients 12 years and older, for on-demand treatment [inaudible] management and routine prophylaxis. Jivi is not indicated for use in hemophilia A patients younger than 12 and previously untreated patients [inaudible] to treat von Willebrand disease. Jivi is a new extended half of recombinant Factor VIII with a unique step [inaudible] prophylaxis dosing regimen. The recommended initial dose is 30 to 40 units per kilo twice weekly. Based on bleeding episodes this regimen may be adjusted to 45 to 60 units per kilo every five days with further individualized dosing adjustments to less or more frequent dosing. [inaudible] data for Jivi shows a mean half-life of 17.9 hours following single dose administration. Efficacy and safety was evaluated in the Protect A trial. One hundred and thirty-two patients received 36 weeks of only mild treatment or 26 weeks of prophylaxis treatment with twice weekly every five days or every seven days regimen. Jivi was effective as routine prophylaxis when administered twice weekly and every five days. The primary efficacy end point, the median ABL was 1.9 for both arms and [inaudible] were reduced by 88.2% when compared to subjects [inaudible]. Forty-six percent and 44% of subjects in Jivi twice-weekly and every five day dosing effectively had no bleeding episodes. The most frequently reported adverse reactions were headache, cough, nausea and fever. One subject had a [inaudible] low [inaudible] inhibitor that was unconfirmed upon repeat testing. An acute hypersensitivity reaction led to discontinuation of two adult subjects, transient anti-pack [inaudible] and antibodies were detected in one of the subjects. Hypersensitivity reactions and [inaudible] of drug effect due to neutralizing anti [inaudible] antibodies were observed in children under the age of 6. Symptoms of these clinical immune responses were transient and occurred in the absence of Factor VIII inhibitors. All subjects transitioned back to their previous factor product. Jivi [inaudible] activity can be analyzed using a validated chromogenic essay or select [inaudible] closing

[inaudible]. Some silica based [inaudible] may underestimate the factor activity. Thank you very much. If you have any questions, please.

Lisa Chew: Thank you very much. The next stakeholder is Dr. Sharon Cahoon-Metzger.

Sharon Cahool: I'm here representing Broveratu and Sanofi and I will [inaudible] my time and thank you for your recommendation [inaudible].

Lisa Chew: Thank you. The last stakeholder is Ms. Stephanie Simpson.

Stephanie Simpson: My name is Stephanie Simpson and I'm the executive director of the Bleeding Disorder Foundation of Washington and we represent the 70,000 patients in Washington with bleeding disorders. Von Willebrand disease is rare, it is 1% of the population. I really just want to say thank you. Thank you to the State of Washington for willing to care for bleeding disorder patients so well because it comes back and it benefits all of us because patients are able to contribute to the society at a much higher level. And thank you for the State to be able to work with the providers so closely. Dr. [inaudible] who is the head of the Washington Center for Bleeding Disorders isn't able to join us today because she got called away with a number of patients, but she too sends her gratitude as do all the medical providers. It really does make it so that when we go out on the national stage and we talk to folks that patients in Washington are living better, higher quality of lives because of this ability for the state and the providers to work so closely together. I just wanted to share a little bit of something that I thought of this morning. And that was my daughter. She's 21 months and fell and really bonked her elbow right in that spot and you're like, "Ugh". And I just thought of all the bleeding disorder patients, because I was able to give her a hug and give her some rubs and say you're going to be okay. If I thought I had a child with a bleeding disorder I probably would have to make a phone call and say I couldn't be here today, because that elbow probably would have blown up with blood and I would have had to make sure she had enough medicine in her body. And I would have had to watch it and her daycare providers wouldn't have wanted her there because they wouldn't have known how to properly treat her. And so I just wanted to share that because, you know, so many of us get to sit here with healthy kids and

healthy family members, and some of us have family members with chronic conditions as well. But I do really say thank you from everyone in the bleeding disorder community for the thoughtfulness that the State providers to bleeding disorder patients.

Lisa Chew: Thank you, Stephanie. All right. So we're going to move to slide 28 where there is a motion.

Amber Figueroa: I move that the Apple Health Medicaid Program implement the limitations for the hematologic agents, anti-hemophilic products listed on slide 27 as recommended.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Okay, Richard, you're on again for hematopoietic agents.

Richard Pope: Thank you. The next is the thrombopoiesis stimulating proteins or the hematopoietic agents.

For overview of the disease state these are platelets. As everyone knows they are small circulating non-nucleated components released into the bloodstream by megakaryocytes. These function to maintain hemostasis by aggregating and forming the platelet plug at the site of injury to limit blood loss. Thrombocytopenia is one of the primary diseases here defined as a platelet count less than 100 x 10^9 per Liter. Thrombocytopenia can result in bruising, bleeding, and fatal hemorrhage. It can result from decreased bone marrow production of megakaryocytes, splenic sequestration of platelets, and increased destruction of platelets. Thrombocytopenia related myelosuppressive chemotherapy often seen after chemotherapy bone marrow production is impaired. Here you have it is not indicated in primary prevention. Neumega is indicated for patients who have experienced severe thrombocytopenia in previous chemotherapy. We'll go to the next slide.

Overview of disease state. ITP, previously known as immune thrombocytopenic purpura. ITP is an immune-mediated disorder in which the platelets are opsonized by autoreactive antibodies and prematurely destroyed by the reticuloendothelial system. Primary ITP, as you will see listed here, is defined by length of time since diagnosis, newly diagnosed or less than 3 months, persistent between 3 to 12 months, and chronic as more than 12 months. Secondary causes include drug-induced autoimmune diseases such as lupus, viral infections such as HIV or Hepatitis C. Severe ITP can occur at any time and indicating bleeding which requires treatment or the occurrence of new bleeding symptoms which requires additional therapy. In children ITP is usually acute and self-limiting. It often occurs two to three weeks after a viral infection or immunization. Spontaneous remission in children is typical occurring, again, between 2 and 8 weeks. Many adult cases are diagnosed incidentally after a routine blood count. Signs and symptoms in adults are highly variable ranging from asymptomatic to mild bruising with mucosal bleeding or to frank hemorrhage from any site. Severity in adults is dependent upon the presence of active bleed, platelet count, age, lifestyle related to risk of bleeding, presence of additional risk factors for bleeding, such as uremia or chronic liver disease. Next slide, please.

Here we have the three main medications seen in this class—Promacta, Neumega and Nplate. None of these are available in generic form or biosimilar form. The indications for each medication are stratified for either ITP or for myelosuppressive agents. As far as the mechanism of action for Promacta it is an oral thrombocytopenia receptor agonist that induces the proliferation and differentiation of megakaryocytes for bone barrow [inaudible] cells. Nplate increases platelet production through binding and activation of [inaudible] receptor in a manner similar to endogenous thrombocytopenia and Neumega stimulates megakaryocytopoiesis and thrombopoiesis. Next slide, please.

On this slide you're going to see the medications, the initial dosing for each medication, titration protocols and availability. Promacta is the only oral medication. Neumega and Nplate are in vials. This class is somewhat unique in that the dosing recommendations may also include notations for race or genetic basis for race. There is likely going to be a

reduction in the initial Promacta dose needed for patients of East Asian ancestry or patients who are East Asian with hepatic impairment. For patients of East Asian ancestry initial Promacta at a reduced dose of 25 mg once daily. For patients of East Asian ancestry with hepatic impairment and [inaudible] classes A, B and C. Prescribers should initiate at a reduced dose of 25 mg once every other day. As far as the specialized population pediatrics safety and effectiveness have not been established in pediatric patients for any products in this category. As seen with the previous two all products in this category are pregnancy category C. For those with renal impairment Neumega is recommended to be dosed by 50%. Patients with severe renal impairment and those with hepatic impairment other than specifically the East Asians, initial dose is recommended for those with [inaudible] A, B or C that it be reduced and after the induction of Promacta and [inaudible] prescribers should wait three weeks before any further increases or titration of Promacta. Next slide, please.

This is the guideline. This is the International Consensus Report from 2010 on Primary ITP. I'll let you read that and take a look at it. Treatment decisions depend on the presence or absence of bleeding, platelet count and assessment of other risk factors. In adults, corticosteroids, particularly prednisone, continue to be first-line for ITP. You also see use of IVIG infusions for certain patients and intravenous anti-RhO (D)/anti-D may be an effective alternative. These can't be used however for Rh-negative or postplenectomy patients. Treatment for patients failing first and second line therapies include thromboplastin receptor agonists, which has some sufficient data support for use and other therapies, which have minimal data to support their use and are considered to have potential for toxicity. Next slide.

Management of ITP. This comes from the American Society of Hematology from 2011. For adults, treatment for newly diagnosed patient is considered to be initiated when the platelet count is below 30 x 10^9 per Liter. Decisions should consider the presence and severity of the bleeding, how rapidly the platelet will rise and possible adverse effects. Next slide, please.

And back to the chair.

Lisa Chew: Thank you, Richard. Any questions for Richard? Okay. There doesn't seem to be any questions. April, do you want to review the policy?

April Phillips: So our recommendation is that all thrombopoietin receptor agonists are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of HCA. And all non-preferred products require a trial of two preferred products with the same indication and different active ingredients before a non-preferred product will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Lisa Chew: Any questions for April? We do have one stakeholder, Dr. Ryan Flynn. Please state your name and who you represent and you'll have three minutes.

Ryan Flynn: Hello. My name is Ryan Flynn. I work with Dova Pharmaceuticals representing Doptelet and avatrombopag which is a new TPO receptor agonist. Doptelet was approved by the FDA on May 21, 2018 for the treatment of thrombocytopenia in patients with chronic liver disease scheduled to undergo a procedure. These can include colonoscopies with or without polypectomies, dental procedures or radio frequency ablations. Thrombocytopenia is common in patients with chronic liver disease and increases in severity with worsening of disease. It presents a significant challenge in patients with chronic liver disease who require multiple invasive procedures [inaudible] carrier risk of bleeding. In fact, several medical societies suggest platelet counts greater than 50,000 prior to conducting these procedures.

The safety and efficacy of avatrombopag were established in two identical randomized double-blind placebo-controlled trials. Adults with chronic liver disease and severe thrombocytopenia who are scheduled to undergo a procedure were divided into two cohorts according to the baseline platelet count. The low baseline cohort we threw patients with less than 40,000 platelet count and received 60 mg or placebo. The high baseline cohort goes with between 40 and 50 platelet count received avatrombopag 40 mg or placebo. Treatment was administered on days 1 through 5 and patients were scheduled to undergo procedure days 5 to 8

after the last dose. In both trials avatrombopag significantly reduced the need for platelet transfusion or rescue procedure for bleeding compared to placebo. Results of a key secondary endpoint also support the efficacy of avatrombopag over placebo. A significantly greater proportion of patients treated with avatrombopag achieved a platelet count greater than 50,000 on procedure day. Overall, the incidence of treatment emergent adverse events were similar between avatrombopag and placebo with the greatest report treatment emergent adverse event being pyrexia, abdominal pain, nausea, headache, fatigue and peripheral edema. There was one treatment emergent adverse event of portal vein thrombosis in an avatrombopag treated patient. Obviously avatrombopag is a thrombopoietin receptor agonist and TPORAs have been associated with [inaudible] complications in patients with chronic liver disease. Portal vein thrombosis has been reported in patients with chronic liver disease treated with TPORAs. By design the duration of avatrombopag treatment effect was measured and transient with platelet counts peaking on the day of procedure and then gradually returning to baseline within 30 days. In conclusion, avatrombopag is a viable alternative to platelet transfusion in patients with thrombocytopenia and chronic liver disease prior to scheduled procedure. Thank you.

Lisa Chew: Thank you, Dr. Flynn. Any questions? Great. Thanks. Okay. Let's move on to the motion. I'm opening it up for discussion or questions or if someone feels comfortable making the motion.

Susan Flatebo: I move that the Apple Health Medicaid Program implement the limitations for the thrombopoietin receptor agonists listed on slide 36 as recommended.

Catherine Brown: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Okay, Richard, back to you. Passive immunizing and treatment agents.

Richard Pope: Thank you. Also known as the immune globulins. The overview for the disease states of these products is used in primary immunodeficiencies which are inherited disorders of the immune system and these predispose patients to increased rate, severity of infections, as well as other possible sequelae autoimmune diseases and certain malignancies. These immunodeficiencies are categorized as humoral or antibody deficiencies, cellular deficiencies, innate immune disorders, or a combination of deficiencies. The hallmark of humoral is the recurrent bacterial infection in the upper and lower respiratory tract. Under normal circumstances the body produces a variety of immunoglobulin, IgA, IgG, IgM. For IgG deficiencies, in particular, that increases an individual's susceptibility to a host of different infections. Primary antibody deficiencies, which account for about 50% of the diseases categorized under primary deficiencies or PIDD umbrella, have been characterized by the presence of absence of B cells, as well as the quantity and quality of an individual's IgG pool. In addition to use in PIDD, exogenous immune globulin has been approved for the disorders listed at the bottom of the slide—multifocal neuropathy, chronic inflammatory demyelinating polyneuropathy, ITP, Kawasaki syndrome, and B-cell lymphocytic leukemia. Next slide, please.

Here we have the medications listed in this class and the respective indications. They are stratified by being ungenerous subcutaneous or both. Again, there are no generics or biosimilars available at this time in this class. The IV formulations include Bivigam, Carimune, Flebogamma, Gammagard, Gammaplex, Octagam, Privigen, and the IV or subcutaneous are Gammagard, Gammaked and Gamunex. Next slide, please.

Here we have the FC formulations only. The subcutaneous formulations, excuse me, are Cuvitru, Hizentra and Hyqvia. Next slide.

Here we have the dosing and availability for both. ITP we talked about. PHI is primary humeral immunodeficiency. MNM as we mentioned is the multifocal motor neuropathy. [inaudible] is a chronic lymphocytic leukemia. Please note to use caution in pre-existing renal insufficiency patients who are not volume depleted. Administer at an infusion rate that is practical for patients at risk of renal dysfunction or thrombotic

events. This class does carry a boxed warning. Labels for all IV sub-q and IM immune globulin products were updated in 2013 to carry the risk of thrombosis for these products. Thrombosis risk factors include advanced age, prolonged immobilization, hypercoagulable conditions, history of venous arterial thrombosis, use of estrogens in [inaudible] catheters, hyper viscosity or other cardiovascular risk factors. And of course thrombosis may occur in any patients receiving these products without any of the identified risk factors. Next slide, please.

We continue to see dosing and availability. It's just some additional notes. For pediatric patients Gamunex 5% is indicated for placement therapy in patients 2 years of age and older with PHI. But Gammaplex 10 is approved for use in adults only. [inaudible] gama 5 has been determined to be efficacious for preventing serious bacterial infections in children with primary immune deficiency age 2 to 16. The safety of [inaudible] 5% in pediatric patients below the age of 2 has not been established. And for the 10% it is approved for chronic primary immuno [inaudible] in patients 2 years of age and older. Bivigam has been studied in children with PHI age 6 and over. Gammagard SC is indicated as replacement therapy for primary humeral [inaudible] deficiency in pediatric patients 2 years and older. Safety and efficacy of Gammagard in patients below the age of 2 has not been established. For Privigen it has not been established in patients with PI who are under the age of 3 for their safety and efficacy and the safety and effectiveness of Cuvitru is approved for use in patients 2 years and older. Safety of Hyqvia in children has not been established and the administration of [inaudible] in pediatric patients with acute or chronic ITP did not reveal any pediatric specific hazards. Next slide, please.

As we continue the dosing and availability for geriatric patients, the other end of the spectrum, there's insufficient numbers generally for geriatric patients 65 and older in most of the trials for these products. While there were no differences in safety and efficacy observed in any trial, there's insufficient data to determine whether they are going to respond differently. For individuals over the age of 65 and for any patient at risk of developing renal insufficiently it is advised and directed that those not be exceeded. The products should be infused at a minimum practical infusion rate. Next slide, please.

More dosing and availability. For pregnant patients these products are generally considered pregnancy category C, which has been discussed before with the exception of [inaudible], Gammagard liquid, Gammaked, Gammaplex 5 and 10% along with Hizentra, Hyqvia and these have not been assigned a pregnancy category but are under that general risk benefit. Cuvitru has not been assigned a pregnancy category. There's no human data indicating risk or potential. For those other specialized patients with renal impairment, individuals at risk for renal insufficiency are at increased risk for complications with the use of immune globulins. Next slide, please.

Here are the guidelines listed in table format. These are from the American Academy of Allergy, Asthma and Immunology from 2011. They list the eight principles here to support safe and effective use of therapeutic immune globulins. The eight principles include indication, diagnoses, frequency of treatment, dose, through levels for IgG, site of care, route of administration and the product. Next slide, please.

Again the AAAAI and Clinical Immunology Society both support the individualized patient characteristic consideration and direct physician consultation in all situations of product selection. The selecting of product is largely matching the right patient with the characteristics with the properties of the products. That is the last slide for this group.

Lisa Chew: Thank you. Any questions? Okay. There are no questions. So, April, do you want to…

April Phillips: The IBIGs prior to we had it spread across two therapeutic classes. The passive immunizing and treatments agents for immune serums and the passive immunizing and treatment agents' combinations. When we looked at it, it didn't make sense so we created another subclass. This obviously happened after the agenda was posted. So all of the products previously mentioned is in this one subclass rather than having it combined with the tetanus immune globulins that didn't work for the same indications. So currently the current limitations kind of vary based on plan and our recommendation is that all passive immunizing and treatment agents for IVIG products are considered safe and efficacious

and are eligible for preferred status and grandfathering at the discretion of HCA. And all non-preferred products require a trial of two preferred products with the same indication before a non-preferred product will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Amber Figueroa: What do you guys think about including something in there about… because there are different forms both IV and subcutaneous making sure that at least one is covered in each.

April Phillips: I believe at this time we all have… we have all products are considered preferred. Just to let you know at this time. But the sub-q and the IV… the intravenous routes are all included in one and I think it just depends on the indication.

Donna Sullivan: The subcutaneous can be self-administered, but it's not an injection. It is an infusion where you have multiple patches on different areas of your body and you still get an infusion through those. So it just goes into the subcutaneous areas as opposed to an IV. So it is still an infusion that may or may not require a health professional to assist in administering.

Leta Evaskus: Are there any stakeholders?

Lisa Chew: There are no stakeholders so we can open it up for more discussion, questions, or if someone feels comfortable making the motion.

Virginia Buccola: I move that the Apple Health Medicaid Program implement the limitations for the passive immunizing and treatment agents: IVIG drug class listed on slide 49 as recommended.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Okay, Richard, back to you for endocrine and metabolic agents.

Richard Pope: Thank you. This is under the Magellan growth factors. You'll see on the slide. Next slide.

This is the overview of disease state, the growth factors. Growth hormone insensitivity or insulin-like growth factor IGF-1 deficiency refers to a couple of disorders characterized by the resistance to growth hormone. It can be defined by deficiency in production of growth hormone or peripheral action of IGF-1 on linear growth. Severe IGF-1 deficiency is due to a mutation in the growth hormone receptor or post-growth hormone receptor signaling. Severe IGF-1 deficiency is also characterized by the development of growth hormone inactivating antibody in those pediatric patients with growth hormone gene deletion. Patients are considered to have severe IGF-1 when the following criteria are present: height standard deviation score </= -3, basal IGF-1 standard deviation is </= -3 and normal or elevated growth hormone levels. For HIV lipodystrophy not long after the beginning of combination antiretroviral therapy was found effective for treating HIV patients some adverse effects began to be manifested and these include a metabolic changes, morphologic abnormalities and lipodystrophy. This was particularly seen in HAART therapy. Patients with HIV lipodystrophy were described as having a loss of subcutaneous fat in the limbs, face, and buttocks and an accumulation of fat in other areas of the body particularly the abdominal viscera. Patients who have abdominal visceral increases and the waist circumference increase are then at an increased risk for metabolic syndrome, cardiovascular disease, atherosclerosis and diabetes mellitus. Next slide, please.

Here we have acute products in this category—Increlex and Egrifta. Again, neither has generic availability. In terms of mechanism of action Increlex increases the human recombinant IGF-1, which is essential hormone mediator in linear growth. Growth hormone bind to the receptors and the liver and other tissues. It stimulates and secretes IGF-1 which subsequently results in the patient's linear growth. Egrifta is an analog of growth hormone releasing factor and stimulates the human growth hormone releasing factor receptors with potencies similar to endogenous growth hormone. Growth hormone then effects the

receptors on a variety of different target cells including osteoblast, chondrocytes, hepatocytes, myocytes and neophytes. Next slide.

Here you have the dosing and availability. As far as storage and administration Increlex maintains the stability when it is refrigerated. After opening of the vial it is stable for 30 days if stored in the refrigerator and it should be administered by subcutaneous injection in the upper arm, thigh, buttock or abdomen. And in order to avoid lipohypertrophy the injection site should be rotated. It also should be given within 20 minutes of a meal or snack. If the patient is unable to eat before or after the injection that injection should be withheld and the dosing should not be made up on subsequent doses. For Egrifta it should be stored in the refrigerator until used. Do not return it to the refrigerator once reconstituted and it should be injected subcutaneously into the abdomen. Next slide, please.

Here we have the guidelines for the growth factors for severe IGF-1 deficiency or growth hormone gene deletion. Increlex is the only product available approved for the indication for long-term treatment of growth failure in pediatric patients with severe primary IGF or with growth hormone gene deletion and development… with the development of neutralizing antibodies to growth hormone. Patients with the diagnosis that are not growth hormone deficient and will not respond well to exogenous growth hormone. Likewise, Increlex should not be used as a substitute for patients who require growth hormone therapy. It should not be used in secondary forms of IGF deficiency and before use all thyroid and nutritional issues should be corrected and resolved. It should not be used for weight loss management. For HIV lipodystrophy recombinant human growth hormone has been used with succe4ss in patients with AIDS-related wasting syndrome since it has been shown to improve muscle mass. The study, however, has shown a reduction in visceral adiposity but supra-physiologic levels of IGF-1 and symptoms of excess growth hormone have occurred causing treatment to be stopped. Egrifta does offer specific treatment options for the reduction of excessive abdominal fat in HIV patients with lipodystrophy as it appears to target visceral fat compartment with little effect on subcutaneous fat or fat in the limbs. And that is the last slide for this class.

Lisa Chew: Thank you, Richard. Any questions for Richard? Okay, April, would you like to review the policy?

April Phillips: Yes. For the growth factors in the Apple Health PDL we have it divided up in two different therapeutic classes. The insulin-like growth factors for Increlex and the growth hormone releasing hormones for Egrifta. So the first policy we're going to present is the insulin-like growth factors Increlex. So our recommendation is diagnosis of severe primary insulin-like growth factor one deficiency or growth hormone gene deletion with neutralizing antibodies. Less than 18 years of age and height standard deviation of less than or equal to -3. So all of the following: height standard deviation score of </= to -3, and basal IGF-1 standard deviation of </= to -3, normal or elevated growth hormone, evidence of non-closure of the epiphyseal plate, bone age of < 16 years of age for male and < 14 years of age for female, and normal thyroid function in the range of 0.5 – 0.6. Also, prescribed by or in consultation with a specialist in endocrinology or nephrology, and does not exceed .24 mg/kg/day. And the patient has none of the following: malnourished, active or suspected neoplasia, closed epiphyses and < 2 years of age.

Lisa Chew: Thank you, April. We do have one stakeholder, Mr. Chrsten Schnatwinkel.

Chrsten Schnatwinkel: I don't have anything to add. I would just like to appreciate your consideration and the acknowledgement of adding some additions there. Thank you.

Lisa Chew: We'll open it up for discussion and questions and if someone feels comfortable to make the motion, we can do that.

Diane Schwilke: I move that the Apple Health Medicaid program implement the limitations for Icrelex listed on slides 56-58 as recommended.

Jordan Storhaug: I second.

Lisa Chew: All in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries.

April Phillips: Before we pass it back to Richard can we do the second policy for the next product in this group, the growth hormone releasing hormones or Egrifta?

So our recommendation is a diagnosis of HIV-associated lipodystrophy, excess accumulation of visceral abdominal fat due to HIV-associated lipodystrophy and the following general-specific measurements: For males a waist circumference > 37.4 inches and a waist-to-hip ratio > 0.94. For females waist circumference > 37 inches and a waist-to-hip ratio > 0.88. And documentation of excess accumulation of abdominal fat has impaired function, such as significantly limiting instrumental activities of daily living and tried and failed a comprehensive diet and exercise program with physician and dietician involvement for at least 6 months with patient compliance documented, and </= to 18 years of age or documentation of closed epiphyses and currently receiving and adherent to antiretroviral therapy. Dose not to exceed 2 mg per day, and patient does not have any of the following: active malignancy, pregnancy and disruption of the hypothalamic-pituitary axis due to hypophysectomy, hypopituitarism or pituitary tumor/surgery, head irradiation or head trauma.

Leta Evaskus: Any other stakeholders?

Lisa Chew: No.

Amber Figueroa: I move that the Apple Health Medicaid program implement the limitations for Egrifta listed on slides 60-62 as recommended.

Nancy Lee: I second that motion.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. It looks like we're at break time. Should we just take 15 minutes and come back at 10:35? Great!

Leta Evaskus: Those on the phone, do you want to call back in?

Man: That would be fine.

Leta Evaskus: Okay. So 10:35.

Before we start the December meeting will be Dale Sanderson's last meeting. So in the start of the December meeting I'm going to have you guys meet on a new Vice Chair so start thinking about who you want to nominate. Okay? Thanks.

Lisa Chew: Go ahead, Richard.

Richard Pope: All right. Thank you. The next class we're going to look at… actually, the next two sets of slides we're going to look at are the iron products. We have them broken into parenteral products and oral products. We're first going to look at the parenteral iron products.

As far as an overview of the disease state, iron deficiency enema very commonly seen in those with chronic kidney disease and often times as associated with decreased absorption of iron from the GI tract. There are approximately 10 million people in the United States who are iron deficient and that includes 5 million who have iron deficiency anemia. About 30 to 50% of all anemia in children and other groups is caused by iron deficiency. Iron deficiency anemia signs and symptoms include the list that you see on the slide there. Next slide.

Here for the parenteral irons we have the indications. The abbreviations by the name of the drug are for molecular weight—Dalton's, chronic kidney disease, sodium chloride and D5W. We have some medications that make up this group Injectafer, Triferic, Feraheme, DexFerrum, InFeD, Venofer and Ferrlecit. None of the medications in this group have any generic formulations available. Next slide.

Over the next several slides we're going to show, again, as we have done before, the various medications, specific dosing, some is weight based and their availability. Next slide, please.

And next slide, please.

And the next slide.

Here we have the iron parenteral guidelines. This is from the National Kidney Foundation. Their 2006 quality initiative outcome. Basically the recommendation for use of IV formulation is one of the preferred routes of administration in those patients with hemodialysis-dependent chronic kidney disease and it also is a good alternative for patients with non-dialysis dependent chronic kidney disease or peritoneal dialysis-dependent chronic kidney disease. The route of iron administration can be either IV or oral in patients with non-dialysis-dependent chronic kidney disease or peritoneal dialysis chronic kidney disease due to the lack of really evidence supporting one route over the other. The goal of iron therapy is to achieve and maintain a target hemoglobin range to avoid iron storage depletion and prevent iron-deficient erythropoiesis. Tests should be performed about 1 to every 3 months depending on the patient's hemoglobin level compared to target range to likelihood of blood loss and when initiating ESA therapy. Parenteral iron replacement may be the primary therapy, or it may be used as an adjuvant therapy in patients receiving ESA or erythropoiesis stimulating agents. Use of iron can reduce the requirement for ESA, particularly in patients on dialysis. Due to some safety concerns with ESA there has been an increase recently in utilization of IV iron formulation in patients with non-dialysis-dependent CKD. The seven products do differ in indication, dosage administration in the instance of their adverse effect. Next slide, please.

We will start on… since it appears this is all grouped together we will start, if all right, on the orals.

Lisa Chew: Yes, go ahead.

Richard Pope: These are appendixes only, which just show the products listed in the iron oral class. Next slide, please.

And that is the conclusion of the iron preparations.

Lisa Chew: Thank you, Richard. Any questions? Okay. April.

April Phillips: Okay. So for the Apple… for the iron-containing products on the Apple Health PDL we have it divided across two therapeutic classes. There's the hematopoietic agents iron and the hematopoietic agents hematopoietic mixtures. For… and then you can see the subclasses that hematopoietic agents iron includes both the single ingredient oral products and the single ingredient parenteral iron products. The mixtures includes the combination oral iron products.

Our recommendation is that all iron-containing products within each class are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of HCA. All non-preferred products require a trial of two preferred products within that class and with the same indication and different active ingredients before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Lisa Chew: For the record there are no stakeholders.

Nancy Lee: I have a quick question/clarification on the chart. I just wanted to know what SSB stood for and GEN, just to make sure.

Richard Pope: Yes, thank you. The SSB is a single-source brand. So there are no generics available for that. And the GEN indicates that it is a generic product.

Amber Figueroa: So based on this recommendation let's say someone has, I don't know, perimenopausal bleeding really heavy. They are waiting for a hysterectomy or something or they refuse surgery. And they are on oral iron of which there is only one active ingredient, right? Iron? So then they would not be able to qualify for a parenteral if they had an insufficient response to oral?

April Phillips: So it would… I guess when it says active ingredient it means like ferrous sulfate, ferrous sulfate gluconate.

Petra Eichelsdoerfer: I noticed that he didn't really mention guidelines that relate to use outside of chronic kidney disease and typically the treatment of choice in people who have severe iron deficiency is going to be an oral product and, yeah, they would switch from one… like if they're not tolerating the ferrous sulfate then they would switch to the ferrous gluconate or to the ferrous fumarate or maybe to the… one of the other products, because there are a whole bunch of them.

Susan Flatebo: Is there specific recommendations or guidelines that they have to fail an oral products before they can be put on an IV product?

April Phillips: I'm sorry, can you please re-state that?

Susan Flatebo: Do patients have to fail an oral iron product before they can be prescribed an IV iron product?

April Phillips: Typically, yes. We don't have an existing policy. Hold on and let me confirm with the…

Susan Flatebo: The reason I bring this us is because, you know, it doesn't really address that. It just, you know, says all non-preferred products, a required trial of two preferred products. It doesn't necessarily say in order to be prescribed an IV or an IV iron product you have to have failed an oral.

Donna Sullivan: I think at one point in time we considered putting the parenteral IV products on a prior authorization, but instead of doing that we just put a maximum allowable reimbursement on the medical side for those particular products and so we don't have them on PA. We just only reimburse an average of the cost, which would then direct providers to use the less costly parenteral products. Currently we don't require any trial and fail of an oral iron before they can go to either IV or other administered iron.

Susan Flatebo: I have another question. For pregnant patient is there certain IV parenteral products that are preferred or recommended?

Donna Sullivan: At this point in time they are all open access. We don't prefer one over the other. Maybe that's a question for Rick to answer if there is any parenteral IV product that is preferred for pregnant women over other parenteral IV products… or iron products.

Richard Pope: No, we don't have any that we would recommend as a preferred one over the other. I guess the other thing that… the slightly different fact would be in the prenatal vitamins. There are a number of formulations that have, in prenatal vitamins, that have iron, BHA and different components in the prenatal vitamins. So I would think that unless there is a severe iron deficiency that would require parenteral administration that most pregnant moms would be able to get their iron through a prenatal vitamin. And again there's a multitude of different formulations there. I think some of the statements have been correct. Really there is no… I wish I could say there is a go-to whether it is the different salts of the iron, whether it's ferrous fumarate, ferrous gluconate, ferrous sulfate, but I think it goes back to the tolerability issue and whichever they respond best to as far as the oral products.

Petra Eichelsdoerfer: So when you're talking about the oral products, the biggest issue is how much are they absorbing because a lot of the tolerability is actually based on what is not being absorbed. And in iron sufficiency anemia the body upregulates the number of receptors for absorbing iron. So it's much better at absorbing it to begin with. Typically hematologists are not going to order parenteral until after it is well established that the person is unable to absorb adequate iron. It usually is failure of more than one agent orally. They are usually going to do two or three. The biggest issue has to do with not getting enough of the iron into the person because they're not… either they're not tolerating it or they're not taking it, or the prescribed dose is too low because the amount that they need of elemental iron is typically 100 mg a day if they are down in the sufficiency range or depleted and that's a lot of iron to get into somebody. Your typical prenatal is somewhere in the neighborhood of about 30 mg of elemental iron and so two more dosages of 30 mg or more. And the problem is the better tolerated ones are lower in elemental iron. So it does become a challenge. Generally speaking, again, most hematologists

are not going to want to do parenteral until after it is well established the person can't do parenteral.

Dale Sanderson: Some of the lymphomas actually prevent absorption of iron completely orally. So it has to be given.

Petra Eichelsdoerfer: It's also common for people who have had upper duodenal surgeries like for example the bariatric surgeries to have problems because iron is predominantly absorbed [inaudible] absorbed in the duodenum. So if they have bypassed the duodenum or it's been damaged by disease or injury, anything like that then they are going to have severe difficulty absorbing the iron. Heme iron is different, but the non-heme iron is where it is absorbed.

Susan Flatebo: I move that the Apple Health Medicaid program implement the limitations for the iron-containing products listed on slide 75 as recommended.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Okay, Richard, we're at pediatric vitamin preparations.

Richard Pope: All right. Thank you. Pediatric vitamin preparations. These next two slides are going to be appendixes as was the oral iron slides. So if we go to the next slide we'll see the first page just listing the products available. It indicates in the label name whether it is a tablet, a chew tablet, liquid, the manufacturer is to the right of the drug type. Again, SSB or generic as a single brand. So there is no generic available for it. And then the provider synergy brand name route and that's the specific drop that you would probably see on the package where it would say Aquadeks drops OTC. This just, again, lists those preparations available.

And the second slide for this, again, shows the rest of them. Selection is going to dependent upon the specific components of the vitamin and the tolerability.

Lisa Chew: Thank you, Richard. For the record there are no stakeholders.

April Phillips: So our recommendation for the vitamins pediatric are all pediatric vitamin products are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of HCA. All non-preferred products require a trial of two preferred products with the same indication and different active ingredients before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Amber Figueroa: Is this a nice time to ask about vitamin D supplementation in newborns?

Donna Sullivan: You can ask. Sure. Go ahead. Ask.

Amber Figueroa: I believe that vitamin D supplementation is recommended and not currently covered. So patients are paying for it.

Donna Sullivan: That's actually, I think a fallacy. We do cover vitamin D, but it is in the multi-vitamin vitamin D product. So it is the Tri-Vi-Sol which has A, B, C… or A, D and E, I believe. So we do cover, you know, several of the over-the-counter and prescription multi vitamins that include vitamin D. It's just that we don't have a single vitamin D only product that's available.

Jordan Storhaug: Can you clarify how much vitamin D is in the supplement?

Donna Sullivan: I don't know off the top of my head. I'd have to get back to you. How much vitamin D would you need?

Jordan Storhaug: Well, I'd imagine that it would be 400 to 800 which would be like the recommended or for most people, but if they had, you know, live in the Northwest with not a lot of summer sometimes people can require more than that. But general supplementation would be at those lower levels. I'm guessing that's…

Donna Sullivan: So are you talking about for adults or children?

Jordan Storhaug: For adults.

Donna Sullivan: So for adults we do not cover vitamin D unless they are actually showing signs of a true deficiency. So they have to be symptomatic, not just have low vitamin D. So those are not covered for adults. But for kids we do cover the multi vitamin… the pediatric multi vitamins that include vitamin D.

Petra Eichelsdoerfer: The triple vitamin like the Tri-Vi-Sol brand for kids is essentially 100% of the RDA. I believe it is 200 IUs for children under the age of… I don't remember if it is 2 or 4.

Amber Figueroa: Also addressing the fluoride. I live in a place that believes that fluoridating the water is conspiracy theory or something.

Donna Sullivan: And for kids fluoride is also covered.

Amber Figueroa: As a separate or included in the…

Donna Sullivan: It is covered as its own ingredient.

Susan Flatebo: I just looked it up. Tri-Vi-Sol has 400 units per dose for children or infants. I move that the Apple Health Medicaid program implement the limitations for the vitamins pediatric drug class listed on slide 80 as recommended.

Lisa Chew: I second. All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Okay, Richard. We are now to analgesics/opioids injectables.

Richard Pope: This is our last slides for today. The analgesics and narcotic injectables is Magellan nomenclature and as Lisa said the analgesics opioid injectables. This again is just an appendix listing these. Here you will see a number of

single-source brands, but also in the next several slides you'll see a number of generic alternatives. Next slide.

Again, this lists the drug name, the manufacturer, whether it is generic or not and then the brand route name, which will often be what you see on the package. Next slide.

We go down through the morphines. And the nalbuphines are our last slide. And again, just as a general comment analgesia release is going to be based upon morphine mill equivalence. They are all equally effective although different people react better to different product, but they are all efficacious and all carry essentially the same risks for over-sedation and for potential… in terms of long-term use for potential addiction.

Lisa Chew: Thank you, Richard. There are no stakeholders for the record.

April Phillips: This particular class, the analgesics opioid injectables will not be included with the Apple Health PDL at this time. I just confirmed with Ryan that it is not subject to the opioid policy. So our recommendation is to continue the limitations. Sorry… the current limitations.

Amber Figueroa: I'm sorry, can you clarify what it means that it is not included on the PDL? So patients are not allowed to receive this when they go to the ER?

April Phillips: No. It's just not included in the single PDL. So it won't be across fee-for-service and all of the managed care plans. It's… that's what that means it is not included in the Apple Health PDL. So it will be…

Amber Figueroa: So it is dealt with differently by each different plan?

April Phillips: Right, yeah.

Donna Sullivan: It shouldn't be any different than it is right now is what we're trying to say.

Nancy Lee: I move that the Apple Health Medicaid program implement the limitations for the analgesics opioid injectables drug class listed on slide 86 as recommended.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Okay. Thank you, Richard.

Richard Pope: You are very welcome.

Lisa Chew: So we're going to be moving on to the opioid policy. This is informational and also a discussion. I don't think… there is not a motion to be made for that. So… and Ryan will lead that discussion.

Ryan Pistoresi: I'm here today to present an update on the Medicaid opioid policy. As you may recall, two years ago in October 2016 we brought the initial draft or the initial idea of a Medicaid opioid policy to the DUR board to solicit feedback and to get ideas. Eventually we came back two more times to present some of our alternatives, some of our changes, and then we, you know, kind of with your support we went ahead and implemented an opioid policy about one year ago on November 1, 2017. So the opioid policy has been effective for Medicaid for about one year now and we wanted to take this time to present you an update about the effects of the opioid policy across from Medicaid populations. So the numbers that we're about to present today include not only the fee-for-service population, but our managed care population. So it includes the entire Medicaid population for Washington State.

On the next slide is just a quick overview of today's presentation where we'll go over a little bit of background information about the opioid policy and then review a bit of the data and potentially the dashboard that we have created for the opioid policy. From there then we'll move into ideas for future analyses about the opioid policy and also talk about potential policy updates.

So we'll start off with a review of the opioid policy. But we'll first start with a graphic that we used back in 2016 that shows the disease burden

of the opioid epidemic within Washington State. So this pyramid was developed by the State Department of Health showing that although a lot of the focus is on the number of deaths that occur in Washington that it is just the tip of the iceberg and as we start to look down at some of the other morbidities and other issues related to the opioid crisis we start to see that it actually affects quite a number of people, not only those who are being hospitalized who are even admitted into treatment, but also the number of people who are using opioids non-medically.

On the next slide is the same pyramid, but updated to have the information from 2017 and if you'll notice there are increases in all four categories related to the opioid epidemic. So an increase in the number of deaths, hospitalizations, treatment abuse and non-medical users. So just giving you an idea that from the last three years the situation has gotten worse in terms of the number of these measures. Hopefully we'll start to see these numbers decrease over the next few years as we begin to, you know, learn more about ways to address the opioid epidemic in terms of preventing abuse as well as connecting people who are currently abusing into treatment.

So the policy that we developed was really rooted in both state and federal guidelines. So if you remember from the initial presentations we derived the policy from the 2015 AMDG guidelines, the 2016 CDC guidelines, as well as recommendations from the Bree Collaborative, which is a Washington State collaborative that's local to the area. We also included studies that were published after those guidelines were and two notable ones were the Shaw, et al Study on looking at the likelihood of long-term opioid use based off of the initial opioid prescription. So one that examined that the amount… the length of the initial prescription had a correlation to the risk of… or the likelihood of long-term opioid use. And then a Hill, et al paper on the variation and excessive dosage of opioids for common surgical procedures. So looking at how much opioids were being prescribed following a surgical procedure versus how much of an opioid were being used in that population and looking at the different characteristics of opioid use following general surgeries.

On the next slide is a slide that we used when we presented this opioid policy in September 2017 to providers in the community and to

pharmacists about the policy really documenting what our goals are with the policy and the goals here are to reduce the unnecessary exposure, unused pills in the community, to ensure safe transitions and best practices, to minimize the administrative burden on providers, and to encourage adherence to the guidelines while recognizing that there are indeed clinical needs for exceptions. And so these are really the measures that we wanted to hold this opioid policy to and really the perspective for which we are presenting the data today. So as we go through these measures and through the dashboard we really want to look back and say, you know, "Did we accomplish our goals with this opioid policy for these five items?"

So just a quick summary of the opioid policy. We have two phases to it with one being the acute use phase and the other being the chronic use phase. So the acute use phase is for clients who have used between 0 to 6 weeks of opioids within a 90-day period and this one is the pill limit that we had discussed. So for patients under 21 years of age they are limited to 18 doses or, you know, an example would be a tablet or a liquid dose about 5 ml of liquid. So depending on what form you're using a dose could be, you know, one tablet, one capsule, one suppository or 5 ml of liquid. And then for those 21 and older the limit was to 42 doses. And of course we allow for exemptions. So if they have certain disease states, certain situations like they are in hospice or palliative care, if they are new to the plan and they are a chronic user then they are allowed to continue beyond these limits, or if the provider feels that there is a medical need they are just able to write "exempt" on the prescription and we're able to process this at the pharmacy with an expedited authorization and provide the amount that is written on the prescription.

So there is a lot of flexibility with the acute use phase. But if there is none of that then it is limited to either the 18 doses or to the 42 doses. The other half of the policy is for the chronic use and this is for patients who have 6 weeks or more of opioid use. The way that we allow for continued use beyond 6 weeks is we require an attestation form to be signed by the prescriber. What this is, is just affirming that the prescriber understands that the patient is now transitioning into chronic opioid use and if they want to start titrating them down they have time to do it before they reach that 12-week threshold which has a very high rate of

continuing on to chronic opioid use for one year and three years down the road. So it's a signal to let the provider know if you want to start decreasing and tapering the patient down now is the time to do that. Or if you want to continue that you are continuing to follow best practices as identified by state and federal guidelines.

Just a bit of policy background. As I mentioned we brought this to the DUR board back on October 16th. So if you remember there was the slide from October 19th, so almost two years ago. And then we also presented in January and February and we did solicit… we received a lot of feedback and used that to incorporate into the policy. As you may remember Governor Inslee issued an executive order in October 2016 around the same time that we presented this to the DUR Board of a statewide opioid plan. And so this policy is aligned within that executive order to help reduce the amount of pills in the community. It went effective on November 1, 2017 for Medicaid and then our state-funded self-plan for public employees that went live on January 2, 2018, so earlier this year.

So the next few slides that we have are about the measures of the opioid policy. So on this slide are just a few ways that we measured the opioid policy. The first four are items looking at the effectiveness of the policy so seeing, did we achieve our intended goal… our intended goals of the opioid policy to reduce the pill burden on the community. The adverse events is a measure to see, you know, did we change prescribing behavior in a way such that because of the pill limit providers were now prescribing higher MEDs. So rather than prescribing the hydrocodone 5 mg they were now prescribing the 10 mg and potentially putting our clients at maybe greater risk being prescribed stronger opioids. And we also had a few other process measures that we wanted to measure to see if behavior changed. One of them is did we have clients now pursue cash payment at pharmacies for their opioid prescriptions to circumnavigate the opioid policy and did we change the way that prescribers were prescribing opioids? So were they switching from hydrocodone to an oxycodone? Or anything to that nature.

So on this slide is kind of the first measure for the effectiveness of the policy and this one is measuring the amount of opioid units prescribed for acute use in opioid-naïve patients. And so this really speaks to that first

measure of, you know, reducing the unnecessary exposure and the unused pills in the community. For this chart you will notice that since the policy went effective in November, 2017 we have a two-month lag period to show what the baseline utilization is and then from November 17 onward we have the effect of the policy. On this slide I wanted to draw your attention to the 12 to 20-year-old age group between the mean and the median. So you'll notice that previously in the previous two months the mean prescription was about 22 tablets or 22 dosages and then when the policy went into effect it went down to 18, which is what the limit is. But if you notice some of the months after are a little bit higher and so that does reflect that there are prescribers doing the exempt and prescribing more for certain situations in which the adolescent population does need more than that pill limit. For the median amount you will notice it goes from 20 down to about 18 and then a few months it is down to about 16. So just looking at the population there. It isn't as pronounced for the 21 or older population because that limit was set at 42. If you look across at the mean and the median the mean doesn't reflect too much of a change. The median does go from 20 to about 16, but all the months are pretty much 16. I think if we looked back it would be more of the same. So really showing that this acute pill limit had an effect on the 0 to 11 and on the 12 to 20-year-old populations.

On the next slide is the rate of acute opioid clients. What this measure is, is looking at our general population. Did we change the number of clients that are receiving acute opioid prescriptions with this policy? As you can see the numbers are pretty consistent from the pre-policy and the post-policy phase. So what this tells us is that this policy is not restricting access to opioids for our population. So this is what we would anticipate to see, with this policy, that we're changing the amount that is being described in the prescription, but that there aren't fewer clients getting acute opioid prescriptions.

On the next slide is a similar measure, but this one is looking at the rate of chronic opioid clients. So for this measure we're looking at the amount of clients that are transitioning beyond the six weeks of opioid therapy within that 90-day period or who are continuing to use opioids thereafter. And so for this measure we actually do see a decrease, but I

want to point out the scale at the bottom that we are looking at a change from 225 or maybe 226, rounding up to 211. And so that's not really a strong indicator of a significant change. Yes, Dale, I see that you have a question.

Dale Sanderson: So if we're doing better in terms of the number of pills that we're giving out, why are we doing worse in terms of disease burden outcome?

Ryan Pistoresi: So that's a good question. So this policy went live in 2017 and the measures that I showed from the DOH were from calendar year 2017. So I don't think that this policy or the change maybe in the behavior of prescribing will have an impact yet. But we may start seeing this in future years, especially as I'm sure you'll all aware of the new opioid prescribing rules that will be in effect for your professions for some of you on November 1st, for the rest of you on January 1st. And I think we'll be able to talk a little bit more about that. I have a slide that highlights some of that in relation to this policy. But to your point we haven't started to see an effect statewide, but we're hoping that, you know, with this policy that it is changing some of the behavior of the prescribing and that this will then have a downstream effect to reduce some of the prevention of opioid abuse and we're also working, you know, statewide to get more access to opioid use disorder treatment, which we may be able to present at a future meeting if you're interested.

Dale Sanderson: Thank you.

Lisa Chew: Ryan, could you go back to the last slide? It looks like access… you're not restricting access to the population, but it looks like the number of acute opioid clients is actually going up. Do you have thoughts about that?

Ryan Pistoresi: Yes. So for this slide I think we want to look at the scale again and look at the numbers. So the absolute numbers from September/October is maybe about 390, 380. And then at the upper end of this we're looking at 406, maybe up to 412. I don't know if that is a significant difference. I mean we didn't have a statistical analysis to show if this is a statistically significant increase. But it is, yeah, I will admit that it is going up and I'd be interested to know… you'll see July and August data, you know, when the new residents come in and they may be coming in from out-of-state

and may not be familiar with this if there will be some changes, as well. So we'll continue to monitor this and see how the data changes over time.

The next measure of effectiveness is related to the amount of NSAIDs and acetaminophen prescribed to our patients. So we were curious that if we were restricting the number of tablets or units being dispensed at pharmacies for these clients were we going to see a change in the amount of NSAIDs and acetaminophen for these populations? So what's interesting about this is that we notice a bit of a spike in January and so it's kind of a non-linear direction for this, which we found to be very interesting. There doesn't seem to be any statistically, you know, increase in the amount of NSAIDs or acetaminophen across these populations, but it shows us that there is kind of this peak around January/February and then it kind of comes down. So we're going to continue to monitor this and see kind of what a one-year cyclical pattern there is in NSAIDs or acetaminophen, but we thought that this was just interesting to share. We don't really have a strong conclusion based off of this data on whether this changed prescribing behavior or not. And if you have any ideas for what's happening in January I think we'd be very interested to get your perspective.

Nancy Lee: Does that include both acute and chronic or just…

Ryan Pistoresi: Yes. So this measure included the entire Medicaid population. So this was looking at patients that qualified for both acute and chronic and for patients who did not use opioids, as well.

Nancy Lee: Any thoughts on looking at like other non-opioid prescriptions like gaba, TCAs, those as well to see if there was a spike in those classes rather than NSAIDs and acetaminophen?

Ryan Pistoresi: So that is a great question. One of the things that we thought maybe a confounding variable is that those other medications are used for other indications and so if there were changes in prescribing, you know, related to pain it may be hard to tease out. We could talk about, you know, looking at potentially linking these claims to ICD10 codes, but that would depend on our data team who actually ran this report and created that

for us. I know that they are going through some other measures that they are building for the agency, but that could be something that we could come back at a future time and then present once we have a little bit more information on some of the other non-pain specific medications.

Nancy Lee: For chronic patients you bring up NSAIDs and acetaminophen and they are not… that's not one of the options for them so that's just a consideration.

Ryan Pistoresi: Right. Yeah, so for this measure it's looking at the entire Medicaid population and not just specific to those users. But that's a good point for a future analysis if we're looking at the chronic users it may be interesting to see who has switched from an opioid to another alternative.

Alex Park Ryan, it would be interesting to compare this timeframe with the same months in the prior year just looking at that temporal blip that happens in January. I don't know if that's related to your eyes and treating sore throat pain or if that is arthritis getting worse in the winter, although there is a Medicare study suggesting that that does not necessarily correlate. It would be interesting to compare those two time points year over year.

Ryan Pistoresi: So thank you for that. Yes, I think when we ran the report we just selected the two months prior and now that we're looking at the data and have more data I think we want to look back and kind of have that cyclical pattern where we can see, you know, is this measure in January 2018 what we would have expected under the previous year in January 2017 and then I think that would give us a better way to do a difference in differences analysis where we can then compare likes and likes. But, yes, thank you for that.

Dale Sanderson: Any ideas on how to measure transition from acute pain treatment to chronic pain treatment, maybe individuals that have been using opioids for chronic pain, which is going to… not going to work. Is there some way of measuring that of people going to SSRIs or some other way of monitoring that?

Ryan Pistoresi: So that's a good question and I think for that we'll to do more of a longitudinal analysis to kind of track the patients as they kind of transition since each patient will be unique and they may switching from, you know, certain drugs to other drugs. We do have an idea. So the Bree collaborative does have a lot of opioid measures and some of them that we have in our dashboard today are actually derived from the Bree collaborative so we could look at some of those measures to identify some of these patients that are transitioning and then maybe do more of a longitudinal analysis on them to see if they started on opioids and then they had a tapering period and then switched to an alternative. But right now this is just very high level summary data, but something I think we would be very interested in in continuing to analyze with our populations.

Okay. So on the next slide is one of our first measures for the adverse events. So we were curious with the acute pill limit were we transitioning… or were we changing behavior in such a way that prescribers were shifting to higher MEDs for our populations. And so on this slide we have it broken out by the different age categories and just looking across there doesn't seem to be a very significant change in the MEDs prescribed. In the 21 and older population the mean does appear to slightly change from about 35/34 to about the 37/36, which isn't too much of a significant change and so we feel pretty good about this measure that prescribing behavior hasn't change so that way in order to kind of get around this pill limit they're not changing from the 5s to the 10s and then telling their patients to cut the 10s in half in order to get that 5 dose. So I think this is supportive of kind of the effects that we wanted to see with this policy. So this is a slide that shows how we've linked our prescription claim data with the state's PDMP data. So the PDMP is administered and run by the State Department of Health. And so they get access to all opioid claims that are dispensed to anyone in Washington State. What our prescription claim system shows is anyone that ran a claim on the Medicaid plan. So if they ran it for a fee-for-service or for a Molina or United or CHPW that would get captured in our pharmacy claim system. So what this allows us to see is were there any claims that… any prescriptions that were dispensed to clients that did not show up in our claims system. And so this shows us for people who are Medicaid clients who may be paying cash for prescriptions or potentially using discount cards or other means of obtaining the prescriptions. With

this graph it shows kind of our trend line with that very top line being the overall population and then the red line that is what pharmacies designate as a cash pay versus another type of pay. So what's interesting about this is kind of just making a very general trend line. The trend line actually appears to be going down very slightly for the number of cash pays or mismatched prescriptions from the PDMP versus our claims system. Some interesting things that you may notice is that very minute green spike back around October 1st. You may recall we originally wanted to have the opioid policy implemented on October 1st. We eventually changed that and moved it to November 1st in order to have everything ready to go. So we think around October 1st, after we made the announcement, that some of the pharmacies may have billed that, you know, through Medicaid. So that green is a Medicaid claim for a Medicaid client that did not show up in our claims system. So we're thinking that those may have been the first time that patients may have started paying cash at the pharmacy, which is kind of why that October 1st is the highest amount of overall and then I think since then people have started to learn more about the policy, how to get claims submitted and get the tablets dispensed.

Amber Figueroa: Can you clarify what green represents? I can't see it on the…

Ryan Pistoresi: Yeah, sorry. So the red line, the one that is kind of there in the middle is for the private pay. So the cash, credit card, anytime that a patient does not use any type of insurance or other coverage. The green line is for Medicaid specific and so that line is when a pharmacy has a client's, you know, set as Medicaid and so we really shouldn't see too much of this green line. What we think this is, is potentially split fills. So it's being submitted to the PDMP as a Medicaid claim, but it's not showing up in our claims system.

Woman: Can you point to the one with your cursor?

Ryan Pistoresi: Yeah, so this line here. I forgot about the cursor. So that line there.

The other colors… so the purple is Medicare populations. So those would be our dual eligibles. There is a brownish line that is commercial insurance. So it is very hard to see on this. There is a pink line, which is

the military installations in VA. The gray/slate line is Worker's Comp, so L&I, Labor and Industries. The kind of gold line down at the bottom is the Indian Nations and then we also have a light blue line that is cash pay; although I think when most pharmacies are submitting PDMP data they use code 01 for the private pay, which is the red line in the middle. And the brown at the top if the total. So it is the sum of all the other lines together. And then since this is the newest data it has not necessary been cleaned and linked to that. So there are no issues going on in July. It's just the data hasn't necessarily been cleaned and then linked yet.

Dale Sanderson: It seems like a number of cofounding issues here in terms of people transitioning to heroin, you know, people transitioning a number of different things that wouldn't show up in these numbers other than outcome. Is there any way to capture that? It just seems like that would be a significant issue that would cofound the data that you have.

Ryan Pistoresi: That is a good point and we are looking to partner with the Department of Health for that type of data. So we wouldn't necessarily have, you know, those types of claims in our system so this is really limited to what we see in terms of the pharmacy side and this is more specific to the policy. But into the general opioid, you know, crisis in general we are going to be looking at some of the other measures. To your point we could be looking at potential changes in the amount of heroin users in the community.

Dale Sanderson: Or perhaps heroin overdose ER visits that would document it as a heroin overdose as opposed to Percocet or…

Ryan Pistoresi: That is a good point. We could take a look at some of our ER data and see what type of codes are being submitted and see if there is potentially a change in that.

Dale Sanderson: A generic opioid, what is the specific overdose?

David Johnson: The other comment I would make for the board just as far as… the limiting factor probably for the PMP data is that it is… in my view it is blunt data. It doesn't do a great job necessarily. It's a pretty good job at really teasing out what got billed. There's a code for, you know, when

something is truly… when a point of service pharmacy truly doesn't bill anything that comes across as cash. Did you use a discount card? Frequently that gets captured as a 04 commercial insurance and I've seen Molina claims that I know in our claims systems were paid for us and got captured on the PMP under commercial. There is inherent weaknesses in how finally and accurately the PMP system captures… how exactly it was processed at the point of sale. I just tell people to take it with a grain of salt. If we're trying to investigate something and we think, "Oh, the patient did this or that." You've got to actually call the pharmacy and say, "How do you actually do this?" You can't always rely on the data as far as the categorization.

Petra Eichelsdoerfer: I'm going to reiterate that. There's also some variation in how… what pharmacies consider to be cash and what they consider to be Medicaid. Frequently, if it is managed care, then yes, it's going to be considered commercial actually and not Medicaid. It differs from pharmacy to pharmacy, but typically within a given chain it will be consistent. So you have to… and there are some that their systems are set so that they never ever ever code anything as cash paid. Again, I've called pharmacies and talked to them and they have told me this. So there are multiple limitations to the interpretation on this.

Ryan Pistoresi: Thank you for that. So the last measure that we have today is related to some of the process… or the last measure that we're sharing today is the process measure looking at the opioid prescriptions by percentage. Unfortunately, when we had this slide made it came out very small. And I know it is very challenging to read, but the point that I wanted to make on this slide is that going between the different months we didn't really see a change in the amount… or the composition of the opioids being prescribed. So I can see some of you are squinting your eyes and kind of holding it up to your face. Generally we're seeing about 45% of opioids being prescribed as the hydrocodone 5. The next closest one is the oxycodone. That's just under 30%. So in the 28/29 range. And then, you know, that's about 75% of the opioids that are being prescribed. The rest are much smaller. Tramadol 50 mg is the next highest at 9 to 10% and the hydrocodone 7.5 mg is around 7%. The rest of that there is kind of in the 1 to 0, 2% range. The point of this slide is not necessarily to strain your eyesight or to give you an eye exam, it's more to show that because

of the opioid policy we really haven't seen the provider shift what is the preferred opioid that they prescribe in these situations. So we're still seeing about the same amount of hydrocodone 5s. Still seeing about the same amount of oxycodone 5s. So the policy did not have a change in behavior that way.

Next up is future policy analyses. So as you saw today this was just very high level summary level data. More to see, you know, what did we change in terms of the behavior of prescribers for our population? The next analyses that we have planned are related to the expedited authorizations, as well as the attestation forms. So one of the things we're interested in that we weren't able to present today or share today based off of our claims data is how are these expedited authorizations being used? So when we had the policy implemented for our self-funded public employees plan for UMP they did an analysis that showed that some of the codes were being incorrectly used that some of the members for UMP who had been around for a number of years were actually receiving the new-to-plan code. And so what we did back in May of this year is that we sent messages to pharmacies just letting them know, you know, we found that this code is being incorrectly used for this member and for pharmacies that we saw that had repeated ones we called them and then requested, you know, do you need more information? Are you having trouble with our policy? Things to that nature. So we're doing a similar analysis with our Medicaid population. So we did receive information data from our MCOs and we are currently going through that and identifying how these EA codes are being used in the community. We are also planning a future attestation form analysis to look and see for the clients who are going onto chronic opioid therapy if there is a difference in the way that they are being managed than previously. So we're trying to tease out some of the details for this analysis, but we're very interested to see how our chronic opioid users are being managed in terms of their care. So are there more… potentially are these clients now receiving more services that are identified with these best practices now that we are sending forms that say, "Are you doing this? Are you doing that? Are you doing this? Are you doing that?" And seeing if that is potentially changing how these clients are being managed. So that may be a topic for a future DUR meeting.

So lastly is potential changes to the policy. So as I mentioned at the very beginning, you know, when we put up this policy we solicited feedback. We changed the policy and then implemented it November 1st. That doesn't mean that we are finished with the policy and that we may be looking to potentially align it in some of the other measures. So you may have known that we at Health Care Authority are sending our prescriber reports related to a few different measures that are identified in the pre-collaborative, namely high dose opioid prescribing, chronic opioid prescribing, and co-prescribing of opioids with benzodiazepines and other sedatives. And so these are areas that we may want to explore putting into our opioid policy. We have talked with the State Hospital Association and the State Medical Association and they do have some interest in potentially looking at these, especially as the state opioid rules are going into effect on November 1st and Dec… no, January 1st. November 1st and January 1st. So these are areas that we could be looking at. So there is a new MED recommendation that will be effective for nurse practitioners, osteopathic physicians, osteopathic physician assistants and podiatric physicians on November 1st. On January 1st rules will be in effect for the allopathic physicians and allopathic physician assistants. The dentists, when I checked the website, the DOH website last week they don't have a date, but by law it can be no later than January 1st. So I'm anticipating that the dental rules will be in effect probably January 1st. And it's worth noting that each of the different boards that reviewed these rules and approved these rules for their professions have slight differences between them. So for all the pharmacists in the room you may want to review the DOH website and just kind of see, okay, what can a dentist do that is different than an allopathic physician? Or what is different than a podiatric physician? So there is going to be some differences. They are aligned on a lot of different measures, but there are some nuances that it is worth nothing. The most notable ones that I was able to review are that dentists do have a bit more restrictions than the other professions. We are also potentially looking at maybe adding in some way of controlling coprescribing between the opioids and the benzodiazepines and some of the other sedatives. So like Soma or some of the sedative hypnotics. So the Z drugs. And so we are still evaluating that. As I mentioned we are doing a measure where we've been sending out provider reports, but we

may eventually have that be a measure in the opioid policy. So I'm opening it up to the board for any questions, comments, discussions.

Dale Sanderson: Dentists? Are they included in this?

Ryan Pistoresi: Yes. So dentists are included in this, but due to some of the limitations that we have with assigning the dental code to… taxonomy, thank you. So we have some issues/limitations with taxonomy codes with this data and so we weren't able to break it out by the individual professions and so we're not able to see who are pain specialists, who are oncologists, who are cardiologists, who are PCPs, who are dentists. So that is a limitation. So this is for all professions, the data that we presented.

Nancy Lee: I had a question. Would you be also looking at naltrexone prescriptions?

Ryan Pistoresi: Naltrexone wasn't included as one of the measurements in this since this was specific to the opioid policy. But we are monitoring that elsewhere within Health Care Authority and we could look at presenting that data at a future DUR meeting.

Woman: And also looking at MAT prescriptions and sort of what is the rate of that and providers and…

Virginia Buccola: I don't know if I have a specific question, but I'm really interested in what might happen in terms of supporting providers in situations where there is coprescribing of benzodiazepines by the psychiatric specialist and then pain management by the PCP or pain specialist? The best we can do is check the database and ask the client and reach out for records and I think that's quite a gray area where even though we might use what we've got it's quite hard to verify that indeed you're following best practice. Just a comment.

Ryan Pistoresi: Right. So if you have seen one of the letters that we're sending out for prescribers who have a higher than average number of coprescribed clients we do have some links to resources on that letter, as well as on our website. So that may be the first area that I would recommend to look at to see if there are any resources that are supportive. I do know that it is a bit of a challenge especially since some of these they may not

know what drugs they are taking. They may not know if it is a benzodiazepine, things to that nature. So it is a bit of a challenge. So we are trying to explore different ways of helping support the providers when these situations do occur.

Woman: Are the letters going to prescribers who are caring for clients who are currently being coprescribed, but maybe you're not prescribing both of them? Does that make sense?

Ryan Pistoresi: Yeah. So we are looking at the claims and we are sending the letter to the writer of the opioid prescription, if they do have it…

Amber Figueroa: And the benzo?

Ryan Pistoresi: Not the benzo prescriber. Yeah. So just the opioid prescriber.

Woman: That clarifies that. I haven't seen those letters, but I think that's just because my practice tends to fall on the benzo side, not the opioid side.

Dale Sanderson: I would heartedly second that concern.

Amber Figueroa: I was also going to make that comment when I was doing primary care and had my own patients. The only patients that were being coprescribed were patients who were getting benzos from the psych and I had discussed every case with psych and they wanted to continue to prescribe benzos. Maybe best practice is just making sure that all the prescribers are aware of what the patient is taking.

Ryan Pistoresi: Thank you for that feedback. We will definitely take that back and consider it and what we can do about letting the benzo prescribers also know.

Woman: I don't want to speak for everybody across the state, all psychiatric nurse practitioners, but I will because I have this microphone. I think letters… I don't know if they would be welcome, but I think they help to support providers in educating clients and it's another level of saying formally this is how practices change and this is how I'm going to help… how I can best

help you most safely take care of you. So I would be in support of letters, you know, to benzodiazepine prescribers.

Ryan Pistoresi: The goal of these letters is to provide more information to the prescribers so that they can make informed decisions and they can better understand because we do know it is a very challenging, very stressful, you don't have a lot of time, and maybe checking the PDMP you're not able to necessarily to do that for every client. So this is just to help support that and to give you a little bit more information saying, "You know, were you aware of this going on and providing some of the client names." So that way you have that information to make an informed decision.

Donna Sullivan: I'm hearing, I thought, that maybe you're advocating benzodiazepines are not best practice anymore, that the guidelines have changed or the field has changed…

Woman: I think the field is changing and there is an appropriate time and place for them and an appropriate amount and we are much more aware than we were about coadministration.

Donna Sullivan: So I'm hearing coadministration is definitely a primary concern, but that we should be possibly educating providers of not using benzodiazepines in the first place regardless of whether there is coprescribing.

Woman: Yes.

Donna Sullivan: So I think there are two educational components here.

Woman: And just like with opiates that the situation that calls for the exemption when this is an appropriate use and, you know, we wouldn't recommend the discontinuation.

Dale Sanderson: There's also, you know, a bit ago a warning came out about possible dementia-related benzodiazepine use and that got everyone's attention.

Lisa Chew: I just wanted to say thank you for bringing this information to the board. I thought… I mean I know that there are data challenges, but I think your

analysis was very thoughtful and balanced looking at effectiveness, process measures and adverse events. So I greatly appreciate that.

Ryan Pistoresi: Thank you very much for that. We are happy to be able to present the initial idea of the opioid policy to you two years ago and we are happy to show, you know, what effects this work was able to achieve for our population. I think we're, you know, not necessarily there yet at our goals, but I think we are well on our way there.

Virginia Buccola: I want to add one more thing. This is a reflection from clinical practice over the last year and I think it aligns with the implementation of the policy, but at a clinic level in a large community mental health clinic in Pierce County we're seeing a spike in grievances against providers who are not providing benzodiazepines at the level… the desired level and it's probably at least five times the level of our normal grievance level and I would attribute that directly to a change in opiate prescribing and so people who are using substances for other reasons outside of just anxiety are feeling the pressure and that the trickle down is happening in very real ways. So that's an observation, just a clinical one, from my practice.

Alex Park: I have a comment about the pyramid slides that you had in the beginning about the number of deaths and hospitalizations and so forth. It is sobbing to see the numbers having gone up. I remember… I'm sure many of us read the 2015 [inaudible] guidelines on opiate prescribing and there was this letter from the Secretary of Health that was very positive in that report saying that the number of hospitalizations and overdoses had gone down in the years before the 2015 guideline came out. And so just seeing these numbers here I just find it very sobering. I don't know how to explain it. It certainly suggests that there is more work to do.

Donna Sullivan: I'm wondering if some of that data might be that the deaths… the overdose deaths related to prescription opioids is going down, but the overdoses and deaths related to heroin, which is also an opioid is going up. So I think that is why there is an upward trend. It's just that it switched from being a prescription drug overdose and death to an elicit heroin overdose and death.

Alex Park: I guess that goes back to Dale's point. So when you say opioid overdose hospitalizations and death that includes not just prescription.

Ryan Pistoresi: Yes. In that term opioids is related to prescription opioids, heroin, fentanyl, anything that comes into Department of Health as any type of opioid. And one of the nice things about the DOH website is they actually do have outward facing dashboards and other measures that have this data available. So if you are interested and you do have some I would recommend going to the Department of Health website and looking at some of these measures and it does have a county by county breakdown so I know that we have a diverse representation from across the State of Washington here. If you're interested around the counties that you serve whether you're interested in rural or urban Washington you'll be able to see some of the measures for that. So I would encourage you that if you want to kind of follow-up from this meeting and see how we're doing at a statewide level, our Department of Health website has some excellent resources for you to use.

Dale Sanderson: I have a somewhat sideways comment or question on the availability and cost and consistency in apparatus in terms of Narcan naloxone. There's two main different kind of types that are used and they are different. They have to be used differently. They can be misused in terms of not really being effective. Is there any attempt being made to work on that?

Donna Sullivan: I mean naloxone we have the naloxone nasal spray as preferred and, you know, covered and then there are the injectable naloxone is also preferred. You're holding up your fingers. What are you…

Dale Sanderson: There's two different types of nasal sprays and so… and they are different and awkward. If you're training the public on one or a family member on one, getting the other one as… one has got like a syringe apparatus that you squirt and it has a vaporizer apparatus on it. The other one is just this white… you have to be very careful not to push it at the wrong time. I mean it's not real intuitive.

Donna Sullivan: At this point I think it is the actual brand Narcan nasal spray is what we have as our preferred. I'm not familiar with what they look like so I

couldn't respond to that. But it is Narcan nasal spray is what is preferred on the PDL right now.

Dale Sanderson: And cost wise if I was…

Donna Sullivan: I think they are about $150 for the package of two. They are relatively inexpensive.

Dale Sanderson: $150?

Donna Sullivan: Yes.

Dave Johnson: I mean it's gone up a lot from what it used to be. When they first launched it, it was about $50. The other alternative on the market was the evzio auto injector that talks to you at about $5,000. Of course the lovely thing on that is that product doesn't have a federal rebate so that one will not be covered.

Lisa Chew: Good discussion. Any last comments or questions? Okay. I think we are adjourned. Thanks.