Drug Utilization Review Board

March 21, 2018

Lisa Chew:	Welcome and good morning. We are convening the Washington State Drug Utilization Review Board. I want to remind everybody that this is a recorded meeting, so please state your name before talking into the mike and let's start off with introductions. Maybe from this end of the table?
Lorena Wright:	Hi. I'm Lorena Wright from Coordinated Care.
Petra Eichelsdoerfer:	Petra Eichelsdoerfer, United Healthcare.
David Johnson:	David Johnson, Molina Healthcare.
Fran McGaugh:	Fran McGaugh, Community Health Plan of Washington.
Susan Flatebo:	Susan Flatebo, committee member.
Alexander Park:	Alexander Park, committee member.
Diane Schwilke:	Diane Schwilke, committee member.
Jordan Storhaug:	Jordan Storhaug, committee member.
Dale Sanderson:	Dale Sanderson, committee member.
Lisa Chew:	Lisa Chew, committee member.
Nancy Lee:	Nancy Lee, committee member.
Virginia Buccola:	Virginia Buccola, committee member.
Amber Figueroa:	Amber Figueroa, committee member.
Leta Evaskus:	Leta Evaskus, Health Care Authority.
April Phillips:	April Phillips, Health Care Authority.

Donna Sullivan: Donna Sullivan, Health Care Authority.

Umang Patel: Umang Patel, pharmacist account manager from Magellan Medicaid Administration.

Emily Transue: Emily Transue, Health Care Authority.

Amy Irwin: Amy Irwin, Health Care Authority.

Jose Zarate: Jose Zarate, Health Care Authority.

Mary Fliss: Mary Fliss, Health Care Authority.

Lisa Chew: Great. Thank you. Is there someone on the phone?

Stephanie Christofferson: Hi. This is Stephanie Christofferson, pharmacist with Magellan.

Lisa Chew: Thank you. Umang, who is going to be attending these meetings, could you do a little more in depth introduction about yourself?

Umang Patel: Sure. So I met many of you last month, but my name is Umang Patel. I am from the Bay Area in California and I come from more of a clinical background where I was an ambulatory care pharmacist at Kaiser doing a lot of different clinics ranging from metabolic to HIV, Hep-C, oncology and things like that. And I recently joined Magellan and I will be the primary point person, the pharmacy account manager for Washington State.

Lisa Chew: Thank you very much. Should we move forward with the therapeutic class reviews?

Umang Patel: Okay. So as I had stated my name is Umang Patel. If you go to the next slide we'll be going over the… overview of the disease state. The indications, dosage and formulations and the guideline updates for seven particular classes, today, with the request from some of the board members we will be going into a little bit more

clinical depth as well with a little bit more background information. Next slide.

The first therapeutic class we will be covering are oral anti-allergen medications. Next slide.

So for allergic rhinitis with or without conjunctivitis it effects approximately 30 million people in the U.S. Subcutaneous therapy moving forward I'll be referring to it as SCIT has proven to be effective in the management of allergic rhinitis and asthma since the early 20th century; however, it requires regular injections and carries the potential of service systemic allergic reactions. In 1998 the World Allergy Organization stated that cumulative evidence showed sublingual allergen immunotherapy SLIT to be an appropriate alternative. It can help the onset of new sensitizations and reduce the onset of asthma. Although SLIT is not appropriate as monotherapy for the treatment of asthma. Just to kind of go into the mechanism of action how SCIT does work is it suppresses the allergic TH2 mediated inflammation and increases specific antibody production. SLIT induces the same modest changes, but it has additional local mechanisms in the oral mucosa and the regional lymph nodes, which are more important. Since the oral mucosa is a natural side of immune intolerance, once the allergen is absorbed it crosses over into the mucosa where it helps mature a negative T cell into a more mature T cell that help suppress both the TH1 and the TH2 responses that I told you were seen in SCIT therapy. Next slide.

The four medications here we will be going over. I will be referring to them by their brand name. The first one is Ragwitek, which is immunotherapy for the treatment of short ragweed pollen-induced allergic rhinitis in adults 18 years of age through 65 years of age. We have Oralair, which is immunotherapy for treatment of grass, pollen-induced allergic rhinitis in persons 10 years through 65 years of age. Grastek, the immunotherapy for treatment of grass, pollen-induced allergic rhinitis in persons 5 years of age through 65. And the last is Odactra, which is

immunotherapy for house dust mite-induced allergic rhinitis in patients 18 to 65 years of age. Next slide.

As you can see, for the dosages and availability all options here are available as sublingual tablets. Oralair is also available in immediate release formulation, as well. In terms of pregnancy Oralair and Grastek are both category B. Ragwitek is category C and there is insufficient data currently on Odactra. For pediatrics Oralair… as you saw on the indications Oralair is indicated in patients greater than 5 years of age. The safety and efficacy of Ragwitek and Odactra have not been established in pediatrics. And all four medications have not… the safety and efficacy has not been established in patients greater than 65 years of age. Next slide.

To summary the guidelines, the American Academy of Allergy, Asthma and Immunology in 2017 recommends SLIT should be only used for FDA-approved uses and advises against off-label use of any of their preparations. They approved allergic rhinitis for Oralair, Grastek and Tagwitek at the time. Please note that Odactra was recently approved so that is why it is not listed there. Practice parameters on allergen immunotherapy stressed the importance of appropriate indications, absence of significant comorbid conditions, and patient's ability to comply with allergen immunotherapy. It is stated that SLIT is safe and effective; however, variations in effectiveness have been attributed to the differences in the dose of allergen used. The Head and Neck Surgery Practice Guidelines in 2015 offer SLIT or SCIT for patients who have an inadequate response to pharmacological therapy, with or without environmental controls, and that both forms of immunotherapy have been proven effective in reducing symptoms. Indications for considering immunotherapy include patient preference, adherence, adverse effects of other medications, coexisting allergic asthma, and possible prevention of asthma. Next slide.

Are there any questions?

Lisa Chew: There are no questions.

April Phillips: We're going to go into the policy next. HCA is going to refer to this class as allergenic extracts oral requiring the diagnosis of severe allergen-induced allergic rhinoconjunctivitis or asthma confirmed by a positive skin test or in vitro testing for allergen-specific IgE antibodies. A history of failure of two preferred classes with a trial of at least 30 days, contraindication or intolerance to all of the following classes: intranasal corticosteroids, oral non-sedating antihistamines, intranasal antihistamines or leukotriene modifiers. And each product is not to be used in combination with a similar immunotherapy and the age limits for each product are as follows per labeling. And it is to be prescribed by or in consultation with a specialist.

Any question on the policy?

Amber Figueroa: Yeah. Can you clarify on your second bullet point, on page 8, it says failure of two preferred products or contraindication or intolerance to all. So if I had a patient who tried let's say Claritin and Flonase were preferred and they tried them together for 30 days. Well, do they have to try them together?

April Phillips: Either way. It is just a trial.

Amber Figueroa: Okay. Then could they qualify for this?

April Phillips: Yes.

Amber Figueroa: Okay. When it says two and then it says all it's kind of confusing wordage.

April Phillips: Yeah, it's the trial of two of the preferred classes or a contraindication to all.

Leta Evaskus: Do you want me to change that products to classes?

April Phillips: Sure.

Amber Figueroa: Is it trial of two classes or two preferred products? What if you tried Rhinocort and Flonase?

April Phillips: We're changing it. It should be classes. Flonase and then maybe a Claritin.

Donna Sullivan: I think what we're trying to say is that two products from two difference classes. So it's not two products each from two different classes, but two products and the two products should be from different classes.

April Phillips: Are there any other questions regarding the policy?

Lisa Chew: Thank you. Are there stakeholders?

Leta Evaskus: There are no stakeholders.

Lisa Chew: Thank you. Shall we move forward with the motion?

April Phillips: HCA is recommending that all oral allergenic extract products are considered safe and efficacious and are eligible for preferred status at the discretion of HCA and all non-preferred products require a trial of a preferred product with the same indication before a non-preferred drug will be authorized unless contraindicated or not clinically appropriate.

Donna Sullivan: That should be two preferred products.

Lisa Chew: Should that state two preferred products in different classes?

Donna Sullivan: Yes.

Amber Figueroa: I think this is just referring to this group of Grastek, Oralair or Ragwitek, isn't it? If we're saying a preferred product in that category, or no?

Lisa Chew: I think that's right.

Leta Evaskus: Is this correct, the second bullet?

Donna Sullivan: So that is the question. I believe all of these have… I don't remember which ones have which indications. I was thinking that they are all relatively different. So once we get to… I think that they are all going to be preferred so they will require… we can either leave it at two or one preferred, it doesn't really matter, but that's up to you guys to decide if you want to keep this from two preferreds. When I said, "Tried and failed two preferreds I was thinking about the policy for clinical criteria and not necessarily tried and failed a preferred with the same class."

Jordan Storhaug: I think there was some confusion on what they were. I almost prefer that it goes back to the original wording and then just in our motion say we support the recommendations on slide 8 and then slide 10, because I think on slide 8, you know, seems to communicate fairly clearly what you guys intend to implement.

Leta Evaskus: Do you all agree? Should I make that change? Yeah? Okay.

Amber Figueroa: I think we need to go back to slide 8 and still further clarify, though, when you're ready, Leta. It still says history of failure of two preferred. Do you want to say two preferred… one preferred product in two separate classes? Or something like that. It's still a little bit unclear.

Lisa Chew: Is the committee comfortable with this wording on slide 8? Would someone like to make the motion?

Amber Figueroa: I move that the Apple Health Medicaid Program implement the limitations for oral allergenic agents as recommended to include… oh wait… we did do any amendments. As recommended on slide 8 and 10.

Jordan Storhaug: I second.

Lisa Chew: All in favor say aye.

Group: Aye.

Lisa Chew: All opposed say no. The motion carries.

Umang Patel: Okay. The next therapeutic class we will be reviewing is cystic fibrosis. Next slide.

Cystic fibrosis is a serious autosomal recessive multiorgan disorder. It affects approximately 30,000 children and adults in the U.S. and it is the most common fatal genetic disease in Caucasians. The median survival in patients with cystic fibrosis is approximately 36 years. With current treatments, children are anticipated to live to approximately 40 years of age. Mutations lead to the disease of the exocrine gland function, resulting in the formation of a thick mucus that builds up in the lungs, digestive tract, and other parts of the body. Cystic fibrosis transmembrane conductance regulator, moving forward being referred to as CFTR, functions as a chloride channel. Mutations in the CFTR result in the abnormalities of chloride transport across epithelial cells on mucosal surfaces. The goals of CF treatment include maintaining lung function by controlling infection and clearing mucus in the airway, maintaining appropriate growth by providing nutritional support such as enzyme, mineral and multivitamin supplements, and managing disease complications such as insulin therapy in patients who may develop diabetes. Next slide.

Here we will primarily discuss three main medications: Kalydeco, which the generic name is ivacaftor; and then the other two medications have an ivacaftor in them Orkambi and lumacaftor and Symdeko which has ivacaftor and tezacaftor. To go into the mechanism of action ivacaftor, which is in all three of these is a potentiator of the CFTR protein, a chloride channel on the surface of the cells that we mentioned earlier. This potentiates the channel opening of the CFTR protein which helps facilitate chloride ion transport. That helps the amount of mucus buildup. Lumacaftor, the other component in Orkambi helps improve the conformational stability of one of the CFTR proteins, which

increases the processing and trafficking of the protein to the cell surface, which again increases chloride ion transport. And lastly the tezacaftor component of Symdeko facilitates the cellular processing and trafficking of normal and select mutant forms of the CFTR which increases the amount of protein delivered to the cell surface. Kalydeco here is indicated for the treatment of CF in patients age 2 years and older who have one mutation in the CFTR gene that is responsive to ivacaftor potentiation based on clinic and/or in vitro assay data. Orkambi is indicated for the treatment of CF in patients age 6 years of age or older who are homozygous for the F508del mutation in the CFTR gene. The limitation of use for this specific medication is the safety and efficacy have not been established in patients with CF that have other than homozygous mutation. And for Symdeko it is indicated for the treatment of patients with cystic fibrosis age 12 years and older who are homozygous for the F508del mutation or who have at least one mutation in the CFTR gene that are responsive to tezacaftor/ivacaftor based on its in vitro and/or clinical evidence. Next slide.

Here you have the dosing and availability. All three are available as tablets along with ivacaftor being… Kalydeco being available as oral granules that can be mixed with soft foods or liquids. All doses should be administered with fat-containing food. No advantage of one over the other in terms of dosing frequency. All are b.i.d. dosing. Please note that there are no dosage administrations needed for any form of hepatic… mild hepatic child [inaudible] class A with any of the three agents. But the dose reduction does start at child [inaudible] class B. In terms of renal dosing adjustments, no dose adjustment is recommended for mild to moderate renal impairment in patients with ESRD for all three, but no studies have been conducted for moderate to severe renal impairment. Next slide.

In terms of guidelines, the Cystic Fibrosis Foundation in 2013 recommended inhaled treatments such as tobramycin, dornase alfa, hypertonic saline, corticosteroids, and oral treatments such as antibiotics and corticosteroids for treatment of symptoms,

exacerbations and/or infections. Chronic treatment of ivacaftor for individuals 6 years of age and older with at least one mutation to improve lung function and quality of life and reduce exacerbation. Please note that Kalydeco had not received approval in younger patients greater than 2 years of age or the additional mutations at the time of publication. Also the other two medications Orkambi and Symdeko were not approved in 2013. And then the Clinical Pharmacogenetics Implementation Consortium in 2014 recommend ivacaftor therapy based on CFTR genotype in patients who have cystic fibrosis greater than 6 years of age who are homozygous or heterozygous for the G551D CFTR variant. And they further state that there are no data regarding whether or not ivacaftor can replace other established therapies. Any questions?

Lisa Chew: There doesn't appear to be questions. April?

April Phillips: So we're going to change things around a little bit to make confusion a little less. HCA's recommendation is also cystic fibrosis agents are considered safe and efficacious and are eligible for preferred status at the discretion of HCA. All non-preferred products require a trial of a preferred product with the same indication contraindicated or not clinically appropriate or if there is only one preferred product available.

Donna Sullivan: What we're doing is… I think we got a little confused. We had the recommendation for the PDL selection after we went through the policy and so the recommendation is really about the PDL class and PDL selection and how to do tried-and-failed of preferred and non-preferred. So next we'll go through the actual policy itself. So there still is going to be a coverage policy itself. So I just wanted to clarify that's what we're going to do for the rest of the classes to try to minimize the confusion between what the recommendation is about versus the motion that we're making in general.

Dale Sanderson: I have a question. In the past Mucomyst like acetylcysteine is used a great deal with patients with cystic fibrosis. Is that no longer being used?

Donna Sullivan: It is still covered. I would imagine that it is still used for breaking up the mucus within the lungs when it is necessary. I don't know…

Dale Sanderson: It wasn't listed here. I just wondered.

Donna Sullivan: These are just the drugs that are specific… that are these specific oral products for cystic fibrosis that are in their own class. So, you know, the acetylcysteine is on the PDL. We're just not reviewing it as part of this particular class.

Dale Sanderson: Thank you.

April Phillips: I'm going to go over the policy real quick. For Kalydeco diagnosis of cystic fibrosis with documentation of at least one mutation in the CFTR gene that is responsive to Kalydeco and decline is at least 2 years of age.

For Orkambi diagnosis of cystic fibrosis with a confirmation of two copies of the F508del mutation and then at least 6 years of age.

And for the Symdeko diagnosis of cystic fibrosis and then either a confirmation of two copies of the F508del mutation or documentation of at least one mutation in the CFTR gene that responds to Symdeko and at least 12 years of age.

The next slide is just a reference slide for the current mutations that are responsive to the products.

Lisa Chew: Any questions for April? We have two stakeholders. We have Dr. Lisa Allen followed by Dr. David Ricker. If you could come up to the podium. Please state your name and who you represent and you have three minutes for comments.

Lisa Allen: Good morning. My name is Lisa Allen. I'm with Vertex Pharmaceuticals and I'd like to address the committee about all three of the products that we have available that are under your consideration. I'd like to begin with Symdeko and then field questions for that product and then move on to Kalydeco and finish with Orkambi.

Symdeko is indicated in the treatment of patients with CF ages 12 years of age and older for homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis [inaudible] brain conductance regulator gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence. The efficacy of Symdeko in patients with CF was demonstrated into phase 3 double-blind placebo-controlled trials, which are denoted as trials 1 and 2 in the USPI. Trial 1 included 504 patients age 12 years of age and older for homozygous for the F508del mutation. They were randomized to receive Symdeko or placebo for 24 weeks. The treatment difference between Symdeko and placebo patients for the primary endpoint of the mean absolute change in lung function measured 5% predicted FEV1 from baseline through week 24 with statistically significant of 4 percentage points. Symdeko also demonstrated a statistically significant 35% reduction in the number of pulmonary exacerbations per year compared to placebo which was a secondary endpoint. Trial 2 was an 8-week crossover study in CF patients heterozygous for the F508del mutation and a second mutation believed to be responsive to Symdeko. 244 patients were randomized too and received and sequences of treatment that included either Symdeko, ivacaftor or placebo. The treatment difference between Symdeko and placebo for the primary endpoint of change in percent predicted FEV1 from baseline to the average of weeks 4 and 8 was statistically significant at 6.8 percentage points. Symdeko patients also showed statistically-significant improvement in percent predicted FEV1 of 2.1% percentage points over ivacaftor monotherapy. Symdeko resulted also in an 11.1 point improvement over placebo in the key secondary endpoint in the CFQR respiratory domain score from baseline to the average of weeks 4 and 8. In both trials patients took the

study drug in addition to their other prescribed therapies such as Mucomyst. In trials 1 and 2 improvements in percent predicted FEV1 were observed regardless of age, baseline percent predicted FEV1, sex and colonization with pseudomonas and concomitant use of standard of care medications. Safety was evaluated in three phase 3 trials. Severe adverse reactions whether considered drug-related or not did occur more frequently in Symdeko patients included distal intestinal obstruction syndrome in three subjects. There were no deaths in the placebo-controlled trial. With one death in the open-label extension study due to respiratory failure and influenza in a patient who had discontinued Symdeko seven weeks prior. The safety profile of Symdeko was generally similar across all subgroups of patients, including analysis by age, sex, and baseline percent predicted FEV1.

Lisa Chew: I'm sorry to interrupt. Please wrap up your comments.

Lisa Allen: Thank you. Symdeko should be used in caution with patients with severe hepatic impairment. There is information in the PI on that. And in summary we believe that Symdeko provides a new CFTR modulator treatment option for CF patients age 12 years of age and older with indicated mutations. I'd be happy to address any questions that you have about Symdeko at this time.

Lisa Chew: Thank you, Dr. Allen. Any questions? Thank you.

Lisa Allen: I'll break and let Dr. Ricker provide his comments.

David Ricker: Good morning. My name is David Ricker. I'm the co-director of the CF Affiliate Center at Mary Bridge Children's Hospital in Tacoma. I'm also a clinical associate professor of pediatrics at the University of Washington. I wanted to respond to the gentleman's question from earlier that Mucomyst or acetylcysteine is typically not used any longer in CF. We have better products available.

I've been involved in the care of children with cystic fibrosis for over 30 years. CF is a life-shortening disease that primary affects the lungs and the digestive system. For those with CF the body's ability to digest food and clear mucus secretions from the lungs is severely impaired. Children with cystic fibrosis live with the difficult burden of daily treatment requirements and often suffer from repeated respiratory infections which can lead to frequent need for antibiotics, prolonged hospitalizations and sometimes to early death.

Over recent years several new medications, CF modulators, the ones we are talking about now, have become available for children and adults with CF. These medications make up an entirely new class of medications in that rather than treating symptoms or effect of the disease itself these medications work directly at the cellular level to reverse the process leading to malfunctioning of the CFTR, the protein that doesn't work properly in children and adults with cystic fibrosis.

So starting a little over six years ago ivacaftor, lumacfator/ ivacaftor and tezacaftor/ivacaftor have become available. These new drugs are prescribed only to patients with particular CF mutations and have been a significant breakthrough in treatment. They have been approved for use only after extensive study has demonstrated improvements in FED1 as their measure of lung health, body index as a measure of nutritional health, quality of life measures, and reductions in pulmonary exacerbations. The newest modulator tezacaftor/ivacaftor called Symdeko is a welcome addition to the CF armamentarium in that it has been found to have fewer side effects than Orkambi and has fewer drug/drug interactions than Orkambi. Symdeko also has a greater range of potentially eligible patients compared to Orkambi.

To conclude I would request that the committee make available to all patients with cystic fibrosis the currently available modulator drugs of ivacaftor, lumacaftor/ivacaftor and tezacaftor/invacaftor to be prescribed as per their respective FDA

labels at established cystic fibrosis care centers. Thank you for your attention.

Lisa Chew: Thank you, Dr. Ricker. Any questions?

Amber Figueroa: I actually have two questions. I don't treat patients with CF so I would… is this… I know it's only been out for five or six years, but is this… do people develop resistance to it or is this going to be a life-long treatment for them?

David Ricker: They don't develop resistance like they would say perhaps with an antibiotic. It presumably would be life-long treatment unless something better comes, which may very well happen. But these therapies would be life-long.

Amber Figueroa: What we're considering requiring is that they would require a genetic testing to know that they would qualify for this whereas when we reviewed the Cystic Fibrosis Foundation recommendations it said, "Have one mutation or… through genetic testing or clinical trial," I think is what it said. But all of these are all CF patients genetically tested?

David Ricker: Yes, they are now. It's pretty much a part of the standard of care.

Amber Figueroa: Okay. Good. Thank you.

Lisa Chew: Other questions? Thank you very much. Dr. Allen, my apologies. I didn't realize you had several products to discuss. Go ahead.

Lisa Allen: Thank you very much. So the second of our compounds that I'd like to address is Kalydeco or ivacaftor. It's indicated for treatment in CF patients ages 2 years and older who have at least 1 of 38 CFTR gene mutations that are responsive to ivacaftor potentiation based on clinical and/or in vitro assay data. Kalydeco, as we discussed, targets the underlying cause of CF which is the genetic defect in that CFTR protein by increasing the channel open probability or gaiting to allow increased chloride ion transport in certain cells. My comments today are going to focus

on 28 newly approved mutations for Kalydeco which came in two separate FDA approvals.

In May of 2017 the FDA expanded the indication of Kalydeco to include 23 responsive mutations. This precision medicine decision was based on in vitro data and supported by safety and efficacy data from previously-conducted clinical trials with up to five years of use in patients. Responsiveness to ivacaftor was determined in vitra by using chamber electrophysiology studies using Fisher rat thyroid or FRT cells, each expressing a single mutant CFTR protein. Ivacaftor increased chloride transport by at least 10% of normal over baseline in these cells expressing 1 of 23 CFTR mutations. A 10% or greater improvement over baseline was selected as the threshold because it is predicted or reasonably expected to predict clinical benefit. In addition, 27 mutations were found not to be responsive to Kalydeco and are thus not indicated for treatment and they are listed in the USPI in Section 12.1.

In July of last year the FDA further expanded Kalydeco's indication with an additional five responsive mutations called non-canonical splice mutations. These mutations could not be tested in the FRT assay mentioned previously. To study the clinical efficacy and safety of Kalydeco in people with these mutations a phase 3 randomized double-blind placebo-controlled two period, eight-week crossover design clinical trial of patients with CF was conducted. The trial included patients with CF 12 years of age and older who had an F508del mutation and a mutation predicted by responsive to Kalydeco. The trial is listed as trial 7 in the USPI Section 14.4.

Patients with CF with one of these five spliced mutations were treated with Kalydeco and their mean absolute change in percent predicted FEV1 improved by 5.4% over placebo at the average of weeks 4 and 8. The improvements were also seen in the CFQR respiratory domain score and other endpoints such as sweat chloride and BMI.

There were warnings and precautions associated with Kalydeco provided in the prescribing information in Section 5 and include important information on transaminase elevations, drug interactions with CYP3A inducers and cataracts. The safety profile of CF patients enrolled in trial 7 was similar to that that was observed in our original registry trials.

We estimate there are approximately 1,900 CF patients ages 2 years and older in the U.S. who have one of these 28 newly approved mutations. The complete list of the 38 ivacaftor responsive mutations can be found in the USPI. In summary, Kalydeco is indicated to treat patients 2 years of age and older with CF who have at least 1 of those 38 mutations. Any questions about Kalydeco or ivacaftor?

Lisa Chew: There doesn't appear to be questions.

Lisa Allen: Thank you. Thank you for letting me monopolize this podium as much as I have. The last product that I would like to address is Orkambi, the combination of lumacaftor and ivacaftor. Previously the FDA approved Orkambi in patients ages 12 years and older who are homozygous for the F508del in their CFTR gene. As with all of these products Orkambi is targeting the underlying cause of CF in these patients, the defective CFTR protein.

Today I'm going to summarize new data that supported the approval of Orkambi in pediatric patients 6 to 11 years of age who are homozygous for the F508del mutation. Also, the completed long-term extension data that we have available and an analysis that evaluated the rate of change in lung function decline a nutritional measure for CF patients taking Orkambi compared to a matched control group.

In September 2016 the FDA approved an expanded indication of Orkambi to include the CF patients ages 6 to 11 who carry two copies of the F508del mutation. Based on data from a 24-week open-label phase 3 trial with 58 patients with CF where the primary endpoint was safety. The safety of profile of Orkambi in

those children was similar to those seen in patients 12 years of age and older and the dose of Orkambi as previously described for those children is two tablets every 12 hours with fat-containing food and each tablet contains lumacaftor 100 mg and ivacaftor 125 mg.

In the Extension Study, which was called the Progress Trial it was a 96-week study that was fed from the two Orkambi pivotal studies. It concluded up to 97% of the patients who participated in our pivotal trials and provided up to 120 weeks of clinical data. The primary endpoint of progress was safety and tolerability, which demonstrated that the safety was consistent with that that was reported in the pivotal studies. Secondary endpoints demonstrated a mean percent predicted FEV1 above pre-treatment baseline throughout the Extension Study. BMI continued to improve in the patients that received Orkambi from the onset of the pivotal studies and a sustained reduction in pulmonary exacerbation rates. Data from the Progress Extension Study was used to evaluate the effect of Orkambi on the rate of change in lung function and nutritional measures compared to a matched control cohort from the USCF patient registry. Each patient treated with Orkambi was matched on known predictors of lung disease progression using a propensity score approach with up to five eligible control patients who were at least 12 years of age or older. 455 Orkambi treated patients who met the inclusion criteria were matched with 1,500 control patients. This analysis found that the annual rate of percent predicted lung decline measured by FEV1 was significantly reduced by 42% in Orkambi treated patients compared to the match control group.

I'm going to close my comments here. The annual rate of change in… sorry. Each of these analyses met statistical significance. These rate-of-range estimates were based on measurements spanning different lengths of time for different patients with more patients contributing information in the first year than in the second year. Neither progress nor the rate of change analysis were included in the approved poll prescribing information and the FDA did not consider this information when approving

Orkambi. This information may not meet the FDA definition of an adequate and well controlled study. At the end I'd like to conclude my comments and address any questions you may have.

Lisa Chew: There doesn't appear to be any questions. Thank you very much.

Lisa Allen: Thank you very much.

Lisa Chew: So we have the recommendation on the slide there for the committee members to review and then we can move forward with the motion.

Amber Figueroa: The second bullet point there, trial of a preferred product with the same indication and different active ingredients. Currently all three drugs in this class have one of the same active ingredients. So I don't understand that slide.

April Phillips: I believe the focus on that is the… sorry… the same indication. The different active ingredient would include like the secondary drug and two of the products.

Donna Sullivan: I think also this is a result of this is like our standard motion template and it might not be quite as specific to this class as it is to generally the other classes. I think you could get rid of that if you like.

Amber Figueroa: So let's say we have a cystic fibrosis patient that is 7 years old, but our preferred is the tezacaftor/ivacaftor. The 7-year-old would still be able to get the Orkambi because it's not indicated… the other one is not indicated until you're 12. We'd be able to get a…

Donna Sullivan: That is correct.

Amber Figueroa: Okay.

Leta Evaskus: Should I delete the second bullet?

Donna Sullivan: No, not all of the second bullet, it's just "and different active ingredients" would be deleted from the second bullet.

Diane Schwilke: I will go ahead and make the motion. I move that the Apple Health Medicaid Program implement the limitations for the cystic fibrosis agents as recommended on slide 21. 17 to 21, excuse me.

Susan Flatebo: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: All those opposed say no. The motion carries.

Leta Evaskus: Flatebo did the motion and Schwilke second?

Amber Figueroa: Schwilke did the motion and Flatebo did the second.

Leta Evaskus: Okay. Thank you. I want to make a correction to the last motion you made. I realized I put slide 8 and 10 instead of 8 through 10.

Donna Sullivan: The policy is over certain… several slides. So the recommendation is really just amending the amendment to say the limitations that were presented on 8 and 9 and then the recommendation on slide 10. So that was just an error on our part.

Lisa Chew: Do we have to do the motion again?

Donna Sullivan: I don't think so.

Lisa Chew: Okay. Good. Can we move on to the pituitary suppressive agents?

Umang Patel: Okay. The next therapeutic class are the pituitary suppressive agents. Next slide.

We'll primarily be focusing on four main disease states. The first being central precocious puberty, which I'll refer to as CPP moving forward. CPP refers to the appearance of hormonal and physical characteristics of pubertal development at an earlier age than is considered normal, before the age of 8 in girls and before the age of 9 in boys, gonadotropin-dependent in where the premature activation of the hypothalamic-pituitary gonadal (HPG) axis occurs, it affects roughly 1 in 5,000 to 10,000 children, it can result in premature rapid development of secondary sexual characteristics, and the treatment goal for this is the management of suppression of puberty. The second disease state we will discuss is endometriosis. It is characterized by the abnormal growth of endometrial cells similar to those that form in the inside of the uterus, but in a location outside of the uterus. For example the pelvic cavity, fallopian tube or ovaries. Approximately 10% of women are affected in which the typical age that woman are diagnosed with endometriosis is in their 30s or 40s. The management goals include pain relief and/or enhancement of fertility. The 2010 Management of Endometriosis guidelines, which were reaffirmed in 2016 recommend initial medical treatment; surgical treatment is recommended when there has been an inadequate response to medical treatment. Next slide.

The third disease state will be prostate cancer in which it is estimated the number of new prostate cancers in the U.S. last year in 2017 was approximately 161,000 with the estimated deaths being at 26,000. Treatment decisions are multifactorial depending on assigned risk group at time of initial diagnosis and patient's projected survival based on age and comorbidity. Hormonal therapy, also called androgen deprivation therapy is the mainstay of treatment for metastatic prostate cancer. It helps lower androgen, which is testosterone and dihydrotestosterone levels which cause the prostate tumor to shrink or grow slower. Luteinizing hormone-releasing hormone (LHRH) agonists prevent signaling from the testicles to make testosterone, therefore it decreases circulating testosterone levels. And the last will be uterine leiomyomata also known as fibroids which are benign

tumors that develop in the smooth muscles of the uterus. The true incidence and prevalence in the general female population is unknown because the condition is frequently asymptomatic and therefore not easily identified. Most women affected by uterine leiomyomata are asymptomatic and require no treatment unless rapid growth is observed or there are any reasons to suspect pelvic malignancy. Next slide.

The medications are… the indications will be split amongst the next four slides. As you can see each of the different medications we have, have various FDA approved indication varying from the four disease states that we just went over. To go into the clinical aspect a little bit the mechanism of action for goserelin it is a synthetic decapeptide analog of GnRH, which acts as an inhibitor of the pituitary gonadotropin secretion. Histrelin and implant is a GnRH agonist and an inhibitor of gonadotropin secretions as well. Leuprolide is a synthetic nonapeptide analog of naturally occurring GnRH. Long term therapy inhibits gonadotropin release from the pituitary glands and suppresses testicular and ovarian steroid genesis stopping testosterone production in the testis and estrogen production in the ovaries. Nafarelin is a potent synthetic analog of the natural occurring GnRH and continuous treatment of this will inhibit the stimulatory effect of the pituitary gland and decreasing the release of the gonadotropin luteinizing hormone and follicle stimulating hormone. The last is Triptodur, which is the newest medication recently approved. It is a potent synthetic decapeptide agonist analog of GnRH which through a negative feedback mechanism inhibits gonadotropin secretion and chronic administration results in decreased LH and FH secretions leading to marked reduction of testosterone levels as seen in surgically castrated men. Next slide.

I won't go over the specific dosing and availability, but you can see all of these medications on this slide are for injection or subcutaneous use. Please note that leuprolide, goserelin and histrelin must be administered under the supervision of a physician. Next slide.

Noting here Lupron Depot and Depot pediatric formulations do not contain a preservative thus the reconstituted suspensions should be injected immediately or discarded if it's not used within two hours.

And then the last slide. Here you'll see that Lupaneta Pack is available as injections and tablets. Synarel is a metered spray pump and Trelstar and Triptodur are suspensions for injections. In terms of all four of these slides that show the indications, pediatrics, leuprolide, histrelin, nafarelin and triptorelin are approved for CPP. However, leuprolide, histrelin and triptorelin have not been established in patients younger than two years of age and the product insert on nafarelin does not specify a particular age. Pregnancy… goserelin, leuprolide, the leuprolide norethindrone combo, nafarelin and triptorelin are all category X. For hepatic impairment no dosage adjustment for moderate liver function is needed for Zoladex, leuprolide, nafarelin, histrelin or triptorelin, but it is contraindicated in patients… excuse me, the Lupaneta Pack does not have dosage adjustments for hepatic impairment but it is contraindicated in patients with markedly impaired liver function or liver disease. And there is no renal dosage adjustment needed for any of these as well. Next slide.

The consensus statement from Lawson Wilkins Pediatric Endocrine Society and European Society for Endocrinology in 2009 conclude that all available GnRH agonists are effective despite their different routes of administration, dosing and duration of action. It favors depot products due to increased compliance in patients. However, it does depend on patient preference. Management of endometriosis guidelines by the American College of Obstetricians and Gynecologists in 2010 recommend initial medical treatment as NSAIDs, oral contraceptives, GnRH agonists and progestins for endometriosis. Surgical treatment is recommended when there has been inadequate response to medical treatment and conservative surgery is recommended in which uterus and ovaries are preserved or definitive surgery can be used for removal of uterus with or without the ovaries as well.

The next slide goes into prostate cancer and uterine [inaudible]. For prostate cancer the National Comprehensive Cancer Network in 2017 overviewed the treatment options consisting of active surveillance, radiation therapy, hormonal therapy, chemotherapy, surgery, or a combination of two or more of the previously stated. Androgen deprivation therapy is the mainstay of treatment of metastatic prostate cancer and they recommend administering anti-androgens in conjunctions with LHRH agonists to prevent testosterone from reaching cancer cells. For uterine [inaudible] or fibroids American College of Obstetricians and Gynecologists in 2008 recommended management of symptoms by oral contraceptives and progestin-releasing intrauterine devices also known as IUDs to help reduce menorrhagia, non-steroidal anti-inflammatory drugs for pain management, and mifepristone and GnRH agonists to shrink fibroids. Treatment selection should be based on a woman's preference and desire to uterine preservation and future fertility. Any questions?

Lisa Chew: There doesn't appear to be questions. April?

April Phillips: We are going to jump to slide 36 and do recommendation before the policy. HCA's recommendation is that all pituitary suppressive agents are considered safe and efficacious and are eligible for preferred status at the discretion of HCA. All non-preferred products require a trial of two preferred products before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Amber Figueroa: We've got a lot of leuprolide differing routes of administration. So we may need to address that in the recommendation as to what may or may not be covered or what has to be tried.

April Phillips: So are you thinking of… instead of different active ingredients, different routes of administration?

Amber Figueroa: What do you guys think?

Susan Flatebo: In my experience I know that the sub-q leuprolide is a lot more painful compared to the intramuscular route. So I don't know if that should figure into it. I don't know if you should really separate it based on route either, but maybe they both should be preferred. I don't know.

Lisa Chew: Is there a way you could say at least two different ways of the… how do I say this? Um, two different routes of administration should be on the preferred drug list.

Amber Figueroa: If we don't want to… if it doesn't make a big difference we don't have to address it. I just saw that there were different routes of administration and I don't know if the cost is different or like… I don't know. When you're talking about the kids, you know, I don't know if just the… the kids is IM anyway it looks like.

Nancy Lee: It looks like the difference would be in patients with prostate cancer where it's like sub-q versus IM versus the other indications or IM or depot.

Susan Flatebo: Is a different route preferred? I mean if a doctor prescribed the Lupron would that not be a preferred product? Would they have to have tried the Eligard first? I mean do we know what the preferred product is right now?

April Phillips: At this time I don't know. I don't know if it's going to be presented later this afternoon.

Susan Flatebo: Okay.

Nancy Lee: April, is it in this handout?

April Phillips: That's what I was wondering. On this printout it's just… the products that we have a history of… if there's no history they're not going to be listed on this. I believe it only goes through the antidepressants. So it's probably not on this list or… or addressed at this time.

Susan Flatebo: Maybe we should just take out the second bullet point and have them both be potentially preferred. I believe it's only the leuprolide agents that have two different routes and this would come into question. I don't know what everybody feels about that.

Amber Figueroa: So how do you… how would it read? How would that second paragraph read?

Susan Flatebo: I say take it out and just have it all pituitary suppressive agents are considered safe and efficacious and are eligible for preferred status at the discretion of HCA.

Amber Figueroa: Just for the leuprolide? Because there's some other drugs here.

David Johnson: As far as preferred products, April, in the file I think they have a printout of what we've been working on. Starting on line 2896 everything is listed as being preferred, if that makes a difference.

April Phillips: I believe they are currently preferred status, they just require prior authorization.

David Johnson: Correct.

Nancy Lee: I would propose not taking out the second paragraph more for the future if other agents come into play, but maybe taking out the routes of administration aspect because I'm kind of… I'm reading it as if leuprolide is… that's gonna be the… it's not talking about the routes of administration. It's talking about the actual medication. So regardless of the routes of administration, it should be preferred. That's kind of how I'm seeing it.

Virginia Buccola: While I don't treat children who have precocious puberty, I think one concern I have would be making sure we preserve the providers' options to use a nasal spray and I don't know… I'm not familiar enough yet with our wording to see if that's protected in this. Could any other committee members give me feedback on that?

Susan Flatebo: Maybe you could put in there "and different active ingredients and different route of administration," maybe?

Amber Figueroa: I think we're finding this hard because this is a group of medications that you're treating adult women, adult men and children. So it's hard to make a one standard thing apply across the board.

Emily Transue: The phrasing we just added seems to say they have to have tried two different things from two different routes of administration, which I think was not the intent. I think if there is a concern about preserving access to nasal administration for children you could put that in explicitly.

Virginia Buccola: I would recommend that then, please. Thank you.

Leta Evaskus: So remove "and different routes of administration" and… do you want those a separate sentence?

Virginia Buccola: Yes, please. Could you insert something like "allow for nasal administration for children"? Any feedback from committee members for children?

Lisa Chew: I will just propose it to the committee. What do they think of this wording or this recommendation? Any concerns? We still have to review the policy piece. Right? Maybe we should do that and then we can come back to this.

April Phillips: So for the policy for the pituitary suppressive agents one of the following uses – the central precocious puberty defined… sorry. So one of the following uses – the precocious puberty for sexual maturity at age 8 for girls and 9 for boys, clinical diagnosis confirmed with one of the following: bone age advanced one year or more beyond chronological age, pubertal response to a stimulation lest and the intracranial tumor has been ruled out. And the following baseline labs have been performed.

The next use is for stimulation test for the diagnosis of hypogonadism or precocious puberty. To suppress onset of puberty in adolescents with early onset of puberty on growth hormone therapy. Or to suppress changes that would occur during puberty for gender dysphoria or transgender adolescents.

For the treatment of endometriosis when conventional therapies have been unsuccessful. For the treatment of dysmenorrhea that is refractory to oral contraceptives. For the treatment of women with chronic refractory pelvic pain or dysfunctional uterine bleeding when conventional therapies have been unsuccessful. To decrease endometrial thickness or fibroid size prior to surgery. For the prevention of heavy uterine bleeding during chemotherapy.

For the treatment of hormone-receptor positive cancer. Hormonal therapy for clinical relapse in persons with stage II to IV granulosa cell tumors of the ovary. And finally for treatment-resistant paraphilia. Are there any questions on the policy?

Alex Park: Just a question on slide 34 about the endometriosis policy. So does this mean that we are only approving these GnRH agonists for 12 months?

April Phillips: Typically it is six months and then potentially another six months after that. So for the 12 months of therapy up to the 12 months.

Lisa Chew: Other questions or stakeholders?

Leta Evaskus: There are no stakeholders.

Alex Park: At least in my practice I, you know, we tend to go to GnRH agonists in the severe patients and then if that's not responsive we often move to a aromatase inhibitor, but that can last longer than 12 months, that period of time when you're making decisions. I just want to make sure that patients and providers would have the option to apply for re-approval or prior authorization after 12 months.

April Phillips: Clinical justification is always taken into consideration. So if that information is provided in the prior authorization.

Lisa Chew: Other questions about the policy or the recommendation?

Virginia Buccola: I would have a question about pubertal suppression for gender dysphoria. Is there a limit to the upper age range? For central precocious puberty it looks like 11 and 12 are what is specified. I don't know, again, if that would fall under clinical, you know, be available for clinical judgment.

April Phillips: Are you suggesting before age 11 for girls and age 12 for boys?

Virginia Buccola: That my suggestion in treatment of gender dysphoria would be that it be at the discretion of the provider when the suppression would be stopped, that it may continue beyond age 11 or 12.

April Phillips: So for gender dysphoria?

Virginia Buccola: Yes.

April Phillips: Okay. Is that what you were thinking? Okay.

Virginia Buccola: Could we add "age of discontinuation is up to provider discretion to suppress changes that would occur during puberty for gender dysphoria, transgender adolescents…"? I need someone feeding me.

Amber Figueroa: With age of discontinuation…

Woman: You could say "with duration of therapy up to provider discretion".

Amber Figueroa: Can you go to the recommendation slide?

Lisa Chew: Any suggestions from the committee members about any modifications to the recommendation or the policy? Should we move forward with making a motion?

Virginia Buccola: I'll go ahead and make the motion. I move that the Apple Health Medicaid Program implement the limitations for the pituitary suppressive agents as recommended in slides 32 through 36.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: All those opposed say no. The motion carries. I think we have a 15-minute break. Maybe return back here at 10:30. Thank you.

We're going to go ahead and get started. I think for this next group of therapeutic class reviews we're going to be doing all the reviews together and then we'll do the stakeholder input and then the motions at the end. Umang, you want to take it away?

Umang Patel: Absolutely. The next therapeutic class review we will focus on are androgenic agents, topical only. Next slide.

Male hypogonadism is the primary disease state. It is caused by insufficient production of testosterone and characterized by low serum concentrations and may present as testosterone deficiency infertility or both. Approximately 20% of men ages 60 to 69 years old and 30% of men ages 70 to 79 years old have serum testosterone levels below the normal range. Symptoms at presentation will primarily depend on the patient's age at the time of disease onset and can include impotence, decreased libido, fatigue, loss of energy, mood depression, and regression of secondary sex characteristics. The risks due to male hypogonadism can include osteoporosis, sexual dysfunction, depression, or cardiovascular disease. Next slide.

Here are the main medications we will be speaking of. We have AndroGel, Fortesta, Testim Vogelxo, Natesto, Axiron and Androderm. These are all FDA approved for testosterone replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone such as primary or second hypogonadism either congenital or acquired. The main mechanism of action here… these are all topical androgens that deliver physiological amounts of testosterone to the patient producing testosterone levels correlating with concentration seen in healthy men. Please note that Eli Lilly has announced a discontinuation of Axiron but it is not related to safety or efficacy of the medication. The product may remain until stock is depleted. I will show you on the next slide there is a generic availability. The safety and efficacy in men with age-related hypogonadism or in males less than 18 years of age have not been established yet. Next slide.

Here you can see AndroGel 1%... the various formulations of AndroGel at 1%, 1.62%, Fortesta and Testim all have generic formulations available, as well. As you can also see from the administration most of these medications do come with specific instructions primarily… instructing patients not to apply to the genitalia or specific parts of the body such as the abdomen for Testim. Next slide.

As mentioned earlier, Eli Lilly has announced the discontinuation of Axiron but there is a generic available for Axiron and Vogelxo. There is REMs at this time for all products in this review except for Androderm and Natesto which require medication guides as a component of REMs to be provided to patients using testosterone therapy. In terms of pediatric recommendations none of these agents are approved in patients less than 18 years of age and children should avoid contact with unwashed or unclothed application sites in men using testosterone gel products. All of these are pregnancy category X and there is insufficient… in terms of geriatric recommendations there was insufficient number of patients greater than 65 enrolled in the study to see whether

there was a difference in safety or efficacy. So there is no geriatric dosing recommendations. Next slide.

In terms of guidelines the American Association of Clinical Endocrinologists in 2010 recommend testosterone therapy for symptomatic men with classical androgen deficiency syndromes aimed at inducing and maintaining secondary sex characteristics and at improving their sexual function, sense of well-being and bone mineral density. It is recommended to initiate testosterone therapy using testosterone options on the basis of the patient's preference, treatment burden and cost. The guidelines recommend against using testosterone therapy in patients with breast or prostate cancer, palpable prostate nodule or induration or prostate specific antigen with these given levels or hematocrit greater than 50% or any of these other risk factors. The primary treatment goal is the continuation of normal activities of daily living and decreased risk of secondary complications such as infertility, osteoporosis, fatigue and mood disturbances. Any questions?

Lisa Chew: There doesn't appear to be questions.

Umang Patel: Okay.

April Phillips: So at the end of each presentation we're going to do a recommendation and then after all of the next three classes then we'll go ahead and do a motion.

Leta Evaskus: After the stakeholders.

April Phillips: So for the androgenic agents the… all androgenic agents are considered safe and efficacious and are eligible for preferred status at the discretion of HCA. And all non-preferred products require a trial of two preferred products with the same indication and different active ingredients before a non-preferred drug will be authorized unless contraindicated, or not clinically appropriate.

Amber Figueroa: There can't be different active ingredients.

April Phillips: I was just reading that going that can't be right.

Lisa Chew: Any other modifications to the recommendation? Umang, I think we are going to move on to the hereditary angioedema guideline.

April Phillips: I think we're doing the Gaucher's next.

Lisa Chew: Oh, okay.

Umang Patel: The next topic we'll go over is for enzyme replacement, Gaucher disease.

So Gaucher disease is a hereditary metabolic disorder that is the most common lysosomal storage disorder. It affects approximately up to 1 in 40,000 live births. It is an autosomal recessive condition caused by deficiency of glucocerebrosidase, which is an endogenous lysosomal enzyme and a component of the cell membrane. This deficiency results in abnormal accumulation of glycolipids in the cell lysosomes. Patients who have this can suffer from skeletal disease (including but not limited to osteopenia, fractures, and bone crisis), anemia, hemorrhage, thrombocytopenia, splenomegaly, and hepatomegaly along with growth retardation, which is of particular concern especially in the pediatric population. Type 1 Gaucher disease is non-neuronopathic meaning non-damaging of the nerve… not caused by damage of the neurons in its nature and it is most… it is the most prevalent type. It is most frequently encountered in those of Ashkenazi Jewish descent, occurring in approximately in 1 of 450 in this ethnic group. The goals of therapy are to improve or eliminate symptoms, prevent irreversible damage and to improve the patient's quality of life. Next slide.

The three main medications here we will discuss are Cerezyme, Elelyso and Vpriv. For Cerezyme it is FDA approved for long-term enzyme replacement therapy for pediatric and adults with confirmed type 1 Gaucher disease that results in one or more of

the following conditions: anemia, thrombocytopenia, bone disease, hepatomegaly or splenomegaly. Elelyso is FDA indicated for long-term enzyme replacement therapy for adults and pediatric patients with confirmed type 1 Gaucher disease. And Vpriv is indicated for long-term enzyme replacement therapy for pediatric specifically 4 years of age or older and adults with type 1 Gaucher. Next slide.

The next two we have is Cerdelga, which is indicated for the treatment of adult patients with type 1 Gaucher disease who are CYP2D6 extensive metabolizers, intermediate metabolizers, or poor metabolizers. And these are all now substrate reduction therapy agents. And Zavesca which is indicated for the treatment of adult patients with mild to moderate Gaucher disease for whom enzyme replacement therapy is not a therapeutic option due to constraints such as an allergy, hypersensitivity or poor venous access. These oral substrate reductions therapy agents function as competitive reversible inhibitors of the glucosylceramide enzyme synthase which results in the synthesis of the glycophospholipids. The goal of this treatment is to reduce the rate of this lipid which allows for the residual activity of the glucocerebrosidase enzyme to be more effective. Essentially the substrate reduction therapy agents can allow the accumulation of the liposomes that I explained earlier to be reduced.

In the next slide you can see the dosing and availability. All enzyme replacement therapies are IV. They all require refrigeration and they must be administered under the supervision of a health care professional.

On the next slide for the substrate reduction therapy these are both available as capsules. In terms of pregnancy Cerdelga and Cerezyme are category C. Vpriv and Elelyso have insufficient data but no fetal harm was reported in animal studies and Zavesca does not have… there is no adequate or well-controlled study in pregnant women at this type.

On the next slide in terms of guidelines the International Collaborative Gaucher Group in 2004 recommend ERT for symptomatic pediatric patients as well as for patients with severe disease. They found that Vpriv appears to have comparable efficacy to Cerezyme. Elelyso is only indicated in adults and Cerdelga is FDA approved for first-line use. Depending on the CYP2D6 metabolizer status, Cerdelga offers an oral option in type 1 Gaucher disease compared to current standard therapy of intravenous ERT. And if ERT or Cerdelga is not possible, Zavesca, another oral option, can be used as an alternative for the management of adults with mild to moderate type 1 Gaucher disease. Any questions?

Lisa Chew: Any questions for Umang? April?

April Phillips: So HCA's recommendation for the agents for Gaucher's disease is all agents are considered safe and efficacious and are eligible for preferred status at the discretion of HCA. And all non-preferred products require a trial of two preferred products 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: Would it be most likely that we would have a preferred product both in the substrate reduction therapy, which is oral and the enzyme replacement therapy, which is IV?

Donna Sullivan: Yes. I believe that the oral capsules are… if I remember the policy, was that they were second line to the enzyme replacement, the IV drugs.

Amber Figueroa: Should we state something like that to make sure that there's both an oral and a…

Donna Sullivan: Correct. You can just say we have to have a preferred oral and IV, if you'd like.

Lisa Chew: Any other modifications to the recommendations? Okay, let's move on to hereditary angioedema.

Umang Patel: Okay. On the next slide hereditary angioedema is a rare autosomal genetic disorder that affects between 6,000 and 30,000 individuals in the United States. It is characterized by recurrent episodes of nonpruritic, nonpitting, subcutaneous or submucosal edema involving the skin or mucosal tissues of the upper respiratory and gastrointestinal tracts. Although swelling can resolve spontaneously in several days, without treatment, laryngeal edema may be fatal and the pain of GI attacks can be incapacitating. Symptoms can begin as early as 2 years of age and persist throughout life with unpredictable severity and frequency of attacks. It is thought that minor trauma and stress can lead to an attack; however, many attacks can occur without any apparent trigger. HAE prophylaxis is needed to reduce potential edema caused by a stressor or procedure likely to precipitate an attack (short-term prophylaxis) or decrease the number of severity of angioedema attacks, which is termed as long-term prophylaxis.

On the next slide you'll see the five main medications. We are looking at better indicated. Each one of these has been indicated for a specific age. Kalbitor has been approved by the FDA for the treatment of acute HAE attacks in patients 12 years of age or older. We have Firazyr which is indicated for the treatment of acute HAE attacks in patients aged 18 years or older. We have Berinert which indicated for the treatment of acute HAE facial, laryngeal or abdominal attacks in adults and pediatric patients. The safety and efficacy for prophylactic therapy has not been established here. Cinryze which is indicated for routine prophylaxis against angioedema attacks in adolescents and adults with HAE. And Ruconest which is indicated for the treatment of acute attacks in adults and adolescent patients with HAE. Again, limitation of use here: effectiveness has not been established in HAE patients with laryngeal attacks. Just to give a little bit of clinical information, the mechanism of action of hereditary angioedema is caused by mutations in the C1-inh which is a genetic disorder. This essentially creates, through a snowball

effect, initiation of both inflammation and coagulation pathways which unregulated activity of plasma, which leads to the unregulated activity of plasma kallikrein, which creates excessive bradykinin ingeneration. Bradykinin is a [inaudible] dilator which is thought to be responsible for the characteristic HAE symptoms including localized swelling, inflammation and pain. Kalbitor here is a reversible inhibitor of the plasma protein kallikrein in which bradykinin would be blocked. Firazyr is a synthetic selective bradykinin B2 receptor antagonist and has similar receptor affinity as bradykinin. Berinert and Cinryze are concentrates of human plasma-derived C1 esterase protein. And Ruconest is a recombinant analog of C1-inh. It does come from the milk of transgenic rabbits. I will lead into that on the next slide as to why that is important and all three of these C1-inh products are IV administered.

On the next slide you will see of the five medications I allude to earlier Firazyr and Kalbitor are subcutaneous whereas Berinert, Cinryze and Ruconest are IV. The primary warnings with Ruconest it is contraindicated in patients with allergies to rabbits. Kalbitor does have a boxed warning that it should only be administered by a health care professional with appropriate medical support to manage anaphylaxis and HAE. In terms of pediatric approval Berinert the safety profile was similar to that observed in adults. Ruconest was studied in patients 13 years of age or older and Cinryze has not been established in patients younger than 18. For pregnancy Ruconest is category B in animal studies whereas the remaining four are category C. And there are no hepatic or renal dose adjustments at this time.

On the next slide in terms of the guidelines Hereditary Angioedema International Working Group or HAWK and the World Allergy Organization in 2012 recommended there is no one agent that is recommended over another. They do recommend considering C1-inh which was Berinert, Cinryze and Ruconest, Kalbitor or Firazyr which are all first line agents in HAE treatments and antihistamines, corticosteroids, or epinephrine have little or no clinical benefit for treatment. The U.S. Hereditary Angioedema

Association in 2016 recommends short-term prophylaxis prior to medical, dental, or surgical procedures. There is a need for long-term prophylaxis that should be made on attack frequency, comorbid conditions, access to treatment, and patient experience and preference. Treatment strategies should be individualized based primarily on patient specific factors. And Berinert is currently the only FDA agent approved to treat all pediatric ages and is the preferred treatment of choice for sort-term prophylaxis prior to medical, surgical and dental procedures. Just a notation this title slide should read hereditary angioedema guideline. So please note that on this slide. Are there any questions?

Amber Figueroa: How do you self-administer an IV medication? Do they teach people how to find a vein?

Umang Patel: So they do say that there are… it is possible to have patients to be taught to go ahead and give those, but it is not first line. What they usually recommend is it should be done at least for the first few courses of treatment in the medical office and then patients can receive sufficient training to have it done themselves.

Donna Sullivan: I'm curious if they have a port possibly placed. If you're having an attack I don't know if you could start an IV fast enough.

April Phillips: HCA's recommendation for the hereditary angioedema agents is all agents are considered safe and efficacious and are eligible for preferred status at the discretion of HCA. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated or not clinically appropriate, or only one product is preferred.

Amber Figueroa: Is Cinryze going to always be approved or do we need to say that since it's the only one right now that is recommended for prophylaxis before procedures and also in pediatrics?

Susan Flatebo: I wouldn't think that we would have to call that out because it's the only one with that indication and it would be approved based on that indication. Correct?

Donna Sullivan: That is correct. So are you saying you don't want it on prior authorization? Is that what you're saying?

Amber Figueroa: I'm just thinking it is the only one that treats kids under age 12 and I'm sure most of those 30,000 people periodically have a medical or surgical or dental procedure. So it seems that since that's the only one that's indicated for that that we need to make sure that that is preferred.

Donna Sullivan: Making it preferred does not mean it doesn't require prior authorization to verify the indication and so even if it was not preferred, if it was being used in kids it would be… and there was no other product that had the same indication for the same age it would be approved. But they all will still require prior authorization even if they are preferred.

Amber Figueroa: So if I have this problem every time I go to the dentist I'm going to have to get a prior auth to get this medication?

Donna Sullivan: Not every time. Usually they are for like a year.

Nancy Lee: Question about… it's probably not for this slide, but for the other ones where we kind of talked about in consultation with an allergist or an immunologist would that be in a different slide or…

April Phillips: We presented the policy on this last month and we did ask for prescribed by or in consultation with one of the following: allergist, immunologist, looks like dermatologist, hematologist, pulmonologist, or medical geneticist.

Lisa Chew: I wonder whether we want to consider putting the sub-q med and the IV med as preferred just if a patient has challenges administering the IV route. I think Firazyr is given sub-q.

Donna Sullivan: I think you could just say there needs to be a subcutaneous and an intravenous product preferred. And instead of intervention I would put product… subcutaneous product.

Lisa Chew: Are there other modifications to the recommendations here?

Umang Patel: Okay. The next topic will be movement disorders. Next slide.

The two main disease states we will discuss are Huntington's disease and tardive dyskinesia. Huntington's is a rare and fatal genetic disorder resulting in the neurodegeneration of the brain, which affects over 35,000 people in the United States. As chorea, an abnormal involuntary twisting or writhing movement, becomes more severe, it can interfere with the patient's function. As this disease progresses, chorea is replaced by dystonia and Parkinsonism. Chorea affects approximately 90% of the people that have Huntington's disease. It often develops early, gradually worsens, and plateaus in the late stages. Tardive dyskinesia is defined as the involuntary movements of the tongue, lips, face, trunk, and extremities that occur in patients treated with dopamine antagonist properties. The epidemiology of TD is not well defined as prevalence evaluations are often done in differing settings. It can occur in all ages, but the risk increases with age. It may consist of movements classified as bradykinesia and/or hyperkinesia. And dopamine transporter dysfunction and chronic central dopamine blockade have been hypothesized to play a role in the development of TD, although multiple other pathophysiologic mechanisms have been proposed.

On the next slide we will primarily be going over these three medications – Austedo, Xenazine and Ingrezza. All three of these agents are vesicular monoamine transporter to VMAT inhibitors. Just a little bit of clinical background, these agents decrease the uptake of monoamine such as dopamine, norepinephrine, serotonin and histamine into the synoptic vesicles thus depleting monoamine stores for the nerve terminals. Austedo has been FDA approved for the treatment of chorea associated with Huntington's disease along with the treatment of tardive

dyskinesia. Xenazine has been approved for the treatment of chorea associated with Huntington's disease and Ingrezza for the treatment of tardive dyskinesia. Next slide.

This slide here is just to give you information on dosing availability for Austedo along with the conversion from Austedo to Xenazine as well. I will be going over this slide and the next slide. Austedo and Xenazine are available as tablets whereas Ingrezza is available as a capsule. The table you see on the bottom right hand is just a table on how to switch from Austedo, which is b.i.d. dosing to Xenazine which is one-a-day dosing as well. There's a lot of information on this slide, but it was just for completeness sake. The dosing is very particular here as well for both tardive dyskinesia and Huntington's chorea as well.

On the next slide you'll see the information Xenazine and Ingrezza whereas I did say earlier Austedo and Xenazine are tablets whereas Ingrezza is available as a capsule. There is a black boxed warning for Xenazine Austedo for a warning of depression and suicidality. For pediatric safety and efficacy have not been established in pediatric patients yet. In terms of geriatrics Austedo and Xenazine have insufficient data. Ingrezza did have three randomized control studies done where the results were similar to younger populations and there was no dosage changes noted. In terms of pregnancy Xenazine is category C and Ingrezza and Austedo do not have any recommendations due to limited data. In terms of hepatic impairment Xenazine Austedo are contraindicated in patients with hepatic impairment. Ingrezza recommends dose reduction in moderate to severe hepatic impairment with a Child-Pugh score of 17 to 15. Renal impairment Xenazine and Austedo have no recommendations due to, again, limited clinical studies. Ingrezza has a dose recommendation… dose adjustment for mild to moderate renal impairment, which is defined as a creatinine clearance of 30 to 90 mL per minute and is not recommended in patients with severe renal impairment, which is a creatinine clearance of less than 30. Next slide.

Now the American Academy of Neurology in 2012 recommended for Huntington's disease they recommended Ingrezza up to 100 mg daily for chorea associated with Huntington's disease. However, keep in mind that the other two medications Austedo and Ingrezza were approved in 2017. For tardive dyskinesia if possible, if there is a potential offending agent it should be switched to an alternative with a lower TD risk. The dose should be reduced and the duration of use should be limited to prevent tardive dyskinesia onset. Austedo and Ingrezza had not been addressed in the clinical practice guidelines. Essentially the recommendations do not recommend one treatment over the other and multiple factors must be taken into account such as patient preference, comorbidity and whether or not patients are CYP inducers. Any questions?

Dale Sanderson: You not the QT interval prolongation is an issue with the first medication. Many of the chronically mentally ill patients that we see are on medications that prolong the QT interval. Are the other two agents free of that issue? Or do all of them have QT interval?

Umang Patel: No. All three have been… they found that all three have been led to clinically relevant QT prolongation.

Dale Sanderson: So this is not unique to what you have here?

Umang Patel: No.

Dale Sanderson: Dopamine activity… so are… I mean this is working against the medications that we're using to treat chronic mental illness. Is this… how big of a dopamine effect is there with these medications? A lot of our antipsychotics are, you know, work against dopamine and antagonists and so do these agents tend to increase dopamine levels? Is there any evidence of causing problems with psychiatric symptoms?

Umang Patel: So there is the black box warning that I had mentioned in terms of suicidality. But there isn't… in terms of dopamine, from what I

could see on the package inserts and the studies, there wasn't a significant amount of dopamine increase, from what I can see.

Virginia Buccola: And I only have limited clinical practice experience with these agents. I haven't seen loss of efficacy in terms of increase in psychosis, but I have seen the black box warning to be true in two instances, you know, with an increase in depression.

Umang Patel: Thank you.

Lisa Chew: Other questions for Umang?

April Phillips: For the recommendation all movement disorder agents are considered safe and efficacious and are eligible for preferred status 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 when there is only one preferred product available.

Lisa Chew: Any modifications to the recommendations? Okay. We have… let's see. For these groups… this classes of drugs we have four stakeholders, Dr. Maria Agapova, Dr. Lisa Stroup, Dr. Nami Park and Ms. Lisa Sniderman-King. If you could please come up to the podium, state your name and who you present, and you each have three minutes.

Maria Agapova: Hello. My name is Maria Agapova. I'm with Teva Pharmaceuticals. I'm the medical outcomes liaison and I presented last month. So I'm here today just to answer any questions. Dr. Patel provided a thorough summary of the disease state and the drug class. Again, Austedo, deutetrabenazine is indicated for both tardive dyskinesia and for chorea associated with Huntington's disease. It is supplied in three strengths, 6, 9 and 12 mg with titration schedule and flexibility to adjust the dose to match patients' benefit risk preferences. The box warning applies to the Huntington's disease population and I wanted to note that in the clinical trial experience 58% of the participants

were on antidepressant medication and that actually, in our experience, about 4.4% reported depression in the deutetrabenazine arm while 6.7% reported those symptoms in the placebo arm. So we had a little bit of a flip. Those numbers are really low, two in the deutetrabenazine arm and three in the placebo arm. I'll take any questions from you.

Lisa Chew: Thank you.

Nami Park: Good morning. My name is Nami Park and I'm a medical science director with Pharming Healthcare. I'm here to provide testimony on behalf of Ruconest, which is currently indicated for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema or HAE. It is contraindicated in patients with known or suspected hypersensitivity to rabbits and rabbit-derived products or a history of hypersensitivity reactions, including anaphylaxis to C1 esterase inhibitor preparations. Ruconest is the first and only recombinant plasma-free C1 esterase inhibitor product. It is administered through IV injection and has a rapid onset of relief with a median time of 75 to 90 minutes. It has shown to raise functional C1 levels an activity of C1 esterase inhibitor levels to normal in greater than 94% of patients. In a pivotal randomized placebo-controlled clinical trial 89% of patients achieved symptom relief after one dose of Ruconest. Between the open label extension phase study 97% of attacks were treated with just one dose. Thus in both cases rescue doses were not needed. With respected durability of response in a recently published post-hoc analysis of 68 patients with data available for least 72 hours after receiving a dose of Ruconest the data showed 93% of these patients were free of symptoms or further attacks for at least three days. Although effectiveness was not previously established in HAE patients with [inaudible] attacks in the pivotal trials due to lack of sufficient enrollment, recent pooled analysis from six trials show [inaudible] attack efficacy similar to all other attack locations. Please also consider Ruconest is the only FDA approved product for HAE or pregnancy category B classification.

At the March 2018 meeting of the American Academy of Allergy, Asthma and Immunology a poster on the safety of Ruconest used in eight pregnant women was presented. The authors concluded that the use of Ruconest for attacks in pregnant women was general safe and well tolerated and the births of healthy babies occurred without complications. As a recombinant plasma-free option, Ruconest has no risk of human pathogen transmission unlike other plasma-derived C1 esterase inhibitor agents.

More importantly, in the event this category experiences a shortage, as was reported by the FDA in September 2017 with a plasma-derived C1 esterase inhibitor, Ruconest is available with scalable and reliable supplies. With respect to adverse events and safety Ruconest is well tolerated with a low risk of adverse events. Common adverse events those greater than or equal to 2% reported in all clinical trials were headache, nausea and diarrhea.

In conclusion, I'd like to thank the committee for allowing me to testify and if you have any questions, I'll take them as well.

Lisa Chew: Any questions? Thank you, Dr. Park.

Nami Park: Thank you.

Lisa Stroup: Hi. My name is Lisa Stroup from Neuroclrine Biosciences Medical Affairs. It's nice to see you all again. I was here last month. I'm not going to reiterate that information, but offer a chance to… for you to ask some questions and also go through two quick pieces of data, new data that I wanted to share with you. As you know, Ingrezza is a [inaudible] highly selective VMAT2 inhibitor. Dr. Sanderson, I just wanted to address the dopamine question that you had. So a VMAT2 inhibitor ends up decreasing monoamines. So if you think about it an antipsychotic is blocking… is working at the dopamine… post [inaudible] dopamine receptors to block dopamine. Right? This is actually decreasing the amount of dopamine that ever gets into the synapse. So you could actually think that it is a different way, in some ways, ending up in… not

depleting, but decreasing dopamine in the synapse. Does that make…

Anyway, available in 40 and 80 mg capsules. It's taken once daily with or without food. Labeled warnings for somnolence and potential QT prolongation although it is not expected to be clinically relevant at the approved doses. It does not carry a black box warning for increase suicidality or depression.

I just wanted to really quickly review our 48-week blinded long-term extension trial that recently came out. We looked at… we re-randomized the placebo patients after the six-week double-blind trial to either 40 or 80 mg, slept everybody on the doses that they had been in the first six weeks and then looked out to 48 weeks, did a four-week washout. What we saw was that the decreases on the AIMs were maintained and in some cases extended. So we saw a mean decrease in the 80 mg group at 48 weeks of 4.9 points and 3 points in the 40 mg group. We looked at multiple psychiatric scales and saw no evidence of psychiatric instability. So everything was maintained, depression, mania rating scales, symptoms of… psychotic symptoms, all of that remained stable across that time. During that washout period the AIMs did start to recur towards baseline. So when they were no longer on the valbenazine we saw the AIMs score start to increase again. So the second piece of information I wanted to go over is the newly published proposed changes to the 2013 AAN… American Academy of Neurology guidelines for the treatment of TD. Video [inaudible], et al. they are the original authors and then they were also the ones on this new paper, conducted a comprehensive review through September 2017 in an effort to update these treatment guidelines and the algorithm. So based on new published level A evidence, they have now established that two medications are to be considered first line therapy for TD, deutetrabenazine and valbenazine and state that these must be recommended as treatment. The other VMAT2 inhibitor tetrabenazine has only level C evidence in the literature. They have two class 3 studies and a negative class 4 open label study and is considered by the authors as only possibly effective in the

treatment of TD. So using this new data the author proposes evidence… an evidence-based algorithm for physician guidance in the treatment of TD placing deutetrabenazine and valbenazine as first line treatment for TD. I think that's probably it. So if there are any questions, I'd be happy to answer them. Thank you for your time.

Lisa Chew: Any questions? Thank you Dr. Stroup.

Lisa Stroup: Thank you.

Lisa Sniderman-King: Thank you. I'm Lisa Sniderman-King. I'm with medical affairs Sanofi-Genzyme and I appreciate the opportunity to present today. I was also here at the meeting last month and I won't be reading the same script in the interest of providing value with answering questions perhaps.

The only thing I would appreciate you making the corrections to the recommended policy. And the only thing that I would like to add today is that you did a great review of Gaucher disease and the indications and for the product Cerdelga the dosing is based on CYP2d6 status as you indicated, but also may be adjusted based on drug/drug interactions with concomitant medications. So that would be important to take into account.

I would be happy to take any questions.

Lisa Chew: Any questions. Great. Thank you very much. I think now we will move on to the motions. Is that correct?

April Phillips: If you want to jump back to slide 54 we can do the motion for the agents for Gaucher's disease.

Amber Figueroa: Can we go back to the recommendation? I wanted to re-word that last line. There must be a preferred drug… no. I just had it and forgot it. It just doesn't look right.

Lisa Chew: I think with the hereditary angioedema we had the same issue. Maybe that wording that we used for…

Nancy Lee: Yes. Change to oral.

Amber Figueroa: How about, preferred products must include at least one IV and one oral route of administration or something like that. It's still not clean. Must include at least one IV and one oral product. Is that better?

Nancy Lee: Preferred products must include at least one intravenous and one oral route of administration?

Lisa Chew: Any other modifications to this recommendation? Can we move to the motion?

I move that the Apple Health Medicaid Program implement the limitations for the agents for Gaucher's disease as recommended on slide 53.

Dale Sanderson: I'll second.

Lisa Chew: All in favor say aye.

Group: Aye.

Lisa Chew: All those opposed say no. The motion carries. Any modifications to this recommendation? I liked how we used the wording from the last one in this one.

Amber Figueroa: I move that the Apple Health Medicaid Program implement the limitations for the HAE agents as recommended on slide 60.

Dale Sanderson: I'll second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: All those opposed say no. The motion carries.

Nancy Lee: Did we do the androgen products? Topical androgen products?

April Phillips: No, we have not done a motion on those yet. So if you want to go back to slide 44, the recommendation.

Lisa Chew: Sorry.

April Phillips: It's all right.

Amber Figueroa: Testosterone is not included in this group.

April Phillips: No. This is only the topical products.

Amber Figueroa: So it won't play into whether or not something would be approved. You wouldn't have to try that first before a topical product were approved.

April Phillips: I'm going to say no. We can make note of that. So two preferred oral… or topical products?

Amber Figueroa: I'm just thinking in clinical practice it seems that it is very difficult to get these topical ones covered. So if something is all of a sudden going to flip and make it really easy, and I know they are fairly expensive. I don't know, I'm just thinking about usage and…

April Phillips: I believe that IMs do not require prior authorization, but the topical products do.

Emily Transue: So would that mean that even if these were preferred they could be on prior authorization with a requirement for IM first?

April Phillips: That's correct.

Emily Transue: Do you want us to confirm that and bring that information back? I think that that is the way that this would play out is that the prior authorization on these would have that.

Lisa Chew: Any other modifications to the recommendations before we move to the motion? Let's move to the motion.

Nancy Lee: I move that the Apple Health Medicaid Program implement the limitations for the topical androgenic agents as recommended on slide 44.

Susan Flatebo: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: All those opposed say no. The motion carries. Any modification to the recommendation on the slide? Okay. Let's move to the motion.

Virginia Buccola: I move that the Apple Health Medicaid Program implement the limitations for the movement disorder agents as recommended on slide 68.

Dale Sanderson: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: All those opposed say no. The motion carries. April, we'll move on to the last two drug classes.

Amber Figueroa: I just had a comment and Donna is not here right now, but I find it really difficult when we're addressing a diagnoses that there are only 30,000 in the entire United States. I haven't ever seen that disorder, number one, and number two, for sure not treated it.

And we're making some pretty decisions about they're… they're going to affect a relatively small number of people, but affect them in a big way. And I appreciated that we had someone here that I could ask questions about cystic fibrosis. So I don't know if it's possible… I know it's probably very expensive, maybe we don't have to have someone here in person, but maybe access to someone on the phone during a meeting that we're going to be discussing these diagnoses that are relatively rare that we, as a group, probably have minimal to zero experience with treating. Just a thought.

Emily Transue: We will definitely take that back. I think that is a very appropriate question.

Nancy Lee: To follow up with that if the committee member could get some background information about if a specialist is going to be present about if there are any conflicts of interest, as well, to be disclosed to the committee members would be appreciated.

April Phillips: Any final comments or questions on the previous presentation? So we are going to go with the antifungal topical solution policy, specifically for Jublia and Kerydin. It requires a diagnosis of onychomycosis of toenails due to one of the following. Since I can't say those I'm just going to point to them. And the diagnosis is confirmed by one of the following tests: the potassium hydroxide test, the fungal culture or nail biopsy.

We are also going to request documentation of medical necessity such as a history of cellulitis requiring systemic antibiotic therapy, client is diabetic with additional risk factors for cellulitis, client has a history of peripheral vascular disease, or the client is immunocompromised or experiencing pain or discomfort associated with the infected nail.

We are also requesting a history of failure of two or a contraindication to all of the following: oral terbinafine, oral itraconazole or generic PENLAC. Are there any comments or

questions on the policy? Were there any stakeholders with comments?

Lisa Chew: There's one stakeholder. I'm not sure if it's under antifungal or sinus node inhibitor because they are grouped together. Dr. Sylvia Churchill.

[inaudible]

Lisa Chew: Any questions for April regarding the policy?

Nancy Lee: I move the Medicaid Fee-For-Service Program implement the policy for the topical solution antifungal drug class listed on slides 2 through 4.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: All those opposed say no. The motion carries.

April Phillips: So for the sinus node inhibitor policy there is only one product in this class, Corlanor. With this all of the following are requested: worsening heart failure in a diagnosis of stable, symptomatic chronic heart failure, left ventricular ejection fraction of less than or equal to 35%, currently in sinus rhythm, and resting heart rate of greater than or equal to 70 beats per minute. Also currently taking a maximum tolerated dose contraindication or intolerance to beta blockers.

And finally none of the following that are listed below and prescribed by or in consultation with a cardiologist or cardiac specialist.

Lisa Chew: Any questions from the committee members for April?

Alex Park: On slide 6 I might strike the worsening there. In my opinion this is indicated for…

Leta Evaskus: Could you speak more into the mike? I can't hear you.

Alex Park: I might strike the worsening heart failure on slide 6. In my opinion this is really indicated for stable symptomatic heart failure.

April Phillips: It was worded that way because that's the FDA labeled indication.

Leta Evaskus: Are you getting rid of it? Yes? Get rid of it? Yes? No? Would you still like to get rid of it?

Alex Park: I'm looking up the FDA indication because I was not aware that that was part of the indication. Okay. Sorry. That's okay. Thanks.

Lisa Chew: Any other questions from the committee? Okay. We do have one stakeholder, Dr. Sylvia Churchill. Please come up to the podium, state your name and who you represent and you will have three minutes.

Sylvia Churchill: Hello. My name is Sylvia Churchill. I'm a pharmacist here in Washington State and I currently work for Amgen as a health outcomes and pharmacoeconomic specialist. I signed up to talk about Corlanor or ivabradine in heart failure. Your policy looks great. The… it's basically right in line with our FDA approved indication. It's in line with the way our clinical studies were done and it's in line with big clinical guidelines. So I really have nothing more to add unless you have any specific questions. Otherwise I'll stop here and let you move on with the meeting. All right. Great. Thank you.

Lisa Chew: Thank you very much. We'll move on to make a motion.

Jordan Storhaug: I think I actually agree with Dr. Park's initial part. Going on the FDA described, what they're saying is that the indications to reduce the risk of hyper… of hospitalization for worsening heart

failure and so it's to reduce the worsening heart failure and I believe what it is describing is its uses in patients with stable symptomatic chronic heart failure with left ventricular ejection fracture less than 35%. So the category that I see are people were severe stable heart failure to prevent worsening, not that they should be worsening currently. I am in more agreement with that.

Amber Figueroa: I move the Medicaid Fee-For-Service Program implement the policy for the sinus node inhibitor drug class listed on slides 6 and 7.

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

Group: Aye.

Lisa Chew: All those opposed say no. Okay, the motion carries. I think we're running ahead of schedule, but it's lunch time. Should we take an hour and come back at 12:45?

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

Stephanie: Yes, I can.

Leta Evaskus: Okay. Talk to you in an hour.

Lisa Chew: We're going to go ahead and get started back from our lunch break and turn it over to Donna.

Donna Sullivan: What we're going to do now is go through some of the drug classes that are going to be implement on July 1st. You already have reviewed the drug classes and all the clinical information. If you remember we stopped making actual product selection until we could look at the cost of the drugs and the supplemental rebates that might be provided with them. So now we're bringing back to you just the final decisions that we have come up with. I didn't really know what the best way to review these were. We have slides that… you have a packet of the slides and they show

the drug class and then what's preferred and what's not preferred. And then we also have a big handout that has like 2017 utilization data in it so that if you have questions about, you know, how many people use this, how many people are going to have to switch. We can follow along and you can ask any questions. But this can go as quickly or as slowly as you guys want it to go depending on, you know, questions that you have. I'm not going to read every slide. We'll put it up there and let you guys look at it for a little bit, ask questions if you have any, and then we'll just move on to the next one. So there's really no formal presentation. Any questions? Okay. And then I do want to say one thing that this slide deck, what we realize is we used the utilization file to create the slides. So there might be drugs that are in a class that aren't on these slides and that means that we just don't have any claims for it. So it doesn't necessarily mean that they are not preferred or that they are preferred. It's just that we didn't have a claim for it. So if you have a question about a drug that's not on here I can try to look it up in a different spreadsheet that we have. But I just wanted to let you know that if it's not listed it doesn't necessarily mean that it is not on the PDL or in the class. We realize that and it was too late to make the changes. So just wanted to put that out there. Next slide.

So this is the allergy/rhinitis class. Just looking at the non-sedating antihistamines. The preferred drugs are really the generics and the non-preferreds are mostly the brands, but desloratadine is also just not preferred. The spreadsheet does coincide with the order of the slides. Most of the utilization is actually in the preferred products. The antihistamines are… the label names… there's so many different generics that have different label names. That's why it is so big in our spreadsheet, but the vast majority of the drugs… of the utilization is already in the products that we're selecting as preferred. Any questions?

[inaudible]

Donna Sullivan: I actually brought a ruler, but it's in my bag. If you would like it I will…

Lisa Chew: Just a question about sort of like for example cetirizine there's tablets, their oral solutions. Does that mean it is all preferred solution versus tablets?

Donna Sullivan: Good question. Let me… so the solution… so the cetirizine solution is preferred, yes. So if you look at the top of the spreadsheet you can see that those are preferred. The cetirizine tablets are preferred. Loratadine tablets and solution are preferred. And I think just fexofenadine tablets are preferred. And then the loratadine/pseudoephedrine products are also preferred. And I believe that that's the only combination that's preferred.

Nancy Lee: Just clarification for the preferred status column. So the P is standing for preferred, I'm assuming and then N for non-preferred. What's NC?

Donna Sullivan: NC is not covered. So over-the-counter drugs are an optional coverage category for Medicaid. So we have made the decision that if an over-the-counter drug is not preferred then it's not going to be covered. And the difference would be, in most instances, is that you don't get the tried and failed option. You'd have to go through an exception to rule. And this aligns with how we currently cover the OTC products today. They're not… only the drugs that are listed on our OTC list are actually covered. And you have to get an exception to rule. It's just a fancy word for a little bit harder than just the PA request, to get coverage for non-covered OTC products. Any other questions? Do you want a few minutes to look at it or are you ready to go to the next?

Nancy Lee: It's more getting a bearing on the different abbreviations in your column. So for the grandfathered period what's the difference between an asterisk and a zero?

Donna Sullivan: Okay. Thanks. Let me just… thank you. That's a great point. So the Rx/OTC column tells if it is a prescription or over-the-counter. So an O is over-the-counter and an R is prescription. The multi-

source code Y means it is multi-source. There is M, N and O. An O would be that it is the originator product. So the multi-source brand that has like loss patent. It's the originator product. An N is it is not multi-source and an M means that it is multi-source. You can just ignore this column for most instances. The brand generic just tells you if the drug is considered a brand or generic according to our drug reference table and then the preferred status, what we just talked about NC is not covered. P is preferred. N is not preferred. If there is ever an asterisk it is because that column or that cell used to be blank and in the pivot table it would insert the word blank. So it was really… it cluttered up the table so I just replaced that with an asterisk. So that's what the asterisk means. And then zero means that there is no grandfathering. Six would be grandfathering for six months. A three would be grandfathering for three months, and a 99 would be they are grandfathered in perpetuity meaning that they won't be asked to switch. Where grandfathering for three or six months would mean that they would have to switch after three months or after six months. That we're just kind of pushing the disruption… potential disruption out a few months so that we don't have a big volume on day one of the implementation. The PA flag, again, asterisk means it is blank. So no PA. There will be a Y if there is a PA on these drugs. And then again it is a total count of members that are on that particular product. So the total in the dark lines where you see the non-sedating total that's potentially… that is not a mutually exclusive number. So there could be double counting if a patient is taking more than one of those products. The totals are really at the product level and then of course how much we've paid for those… all of those products is the total.

Amber Figueroa: Going back to the grandfathering, how will that get… will that get communicated in the form of a letter to the provider and the patient like it does now?

Donna Sullivan: Yes. So the letters go out I think 30 or 60 days before the date of the change and then the pharmacies, you know, obviously the… when it expires it will reject at the pharmacy. But they do go out to the provider and to the patient and some of the plans, I think,

are actively trying to switch people over if they know that a grandfathering is expiring.

Amber Figueroa: Is the letter potentially going to say what is covered? That's the most frustrating thing as a provider is you get something back from the pharmacy, "That's not covered anymore." And you're like, "Well, there's 17 other options."

Donna Sullivan: Right. The letters that come from the plans will tell you what will be preferred instead of the drug that's going off the label. We are also having the plans change their messaging when a drug rejects if it's not preferred. Instead of saying like a PA required it's actually telling you what the preferred drugs are. So hopefully the pharmacies will at least have that information to communicate it to you whether or not they do, I don't know. We're making sure that they are giving you the information that is necessary so that the pharmacy can just call and get a new prescription versus saying, "This needs a PA" when it really just needed to be switched to a preferred drug.

Leta Evaskus: I have a question, too. Under allergy rhinitis it says it is grandfathered for 99.

Donna Sullivan: Yeah. That would be for… I'm not sure which one you're looking at.

Leta Evaskus: It's on the third page allergy rhinitis nasal steroids. So for 99 months?

Donna Sullivan: No. 99 means it is grandfathered forever.

Leta Evaskus: Oh, gotcha. Thanks.

Donna Sullivan: Any questions about non-sedating antihistamines or about the… before we move forward? Okay. Hearing none we're going to move forward.

So the next class is the antihistamines other. So these are more the sedating type of antihistamines. So we're preferring the chlorpheniramine maleate 4 mg tablets and then the cyproheptadine diphenhydramine and then all the others listed are not preferred. So again the… most of them are over-the-counter. The diphenhydramine liquid is also preferred, so tablets, and liquid is preferred. There is very little utilization. Again, the reason why there's… it looks like there's very little utilization of non-preferred products is most likely that they are not covered at this point in time. So the majority of the patients, again, are on the covered products and this aligns with what we're… our current OTC coverage for this particular class. Questions? Okay. And if you're thinking of some antihistamines there's others that are used for more antiemetics or are in the antiemetic class. So just in case you were wondering.

Going to the next slide is the nasal steroid… or the saline nasal sprays. So the OTC nasal sprays that are considered generic are preferred and the others will not be preferred. So that's not very exciting to talk about. The next slide.

The ipratropium nasal spray is going to be preferred. I think we can just move along to the next slide.

So the nasal antihistamine so the Azelastine nasal spray will be preferred and all the other… so the generic will be preferred and all the others are not preferred. We're not grandfathering these drugs. Again, the majority of the utilization lines up with what's already preferred. Any questions?

Moving on to the nasal steroids. So we're preferring the budesonide nasal spray, the fluticasone propionate nasal spray, and the triamcinolone nasal spray. Again, pretty much lines up with utilization, not grandfathering this class. Any questions? Okay.

Moving on them to the allergens, the allergy extracts. So the Adagen and Grastek are preferred. I did just look. These don't

have federal rebates. So I don't know if they did last year and that's why they were preferred, but drugs that don't have federal rebates are not covered by Medicaid. So the drugs that we looked at in the policy today or in the drug class today only one of those, and I think it was the one that started with O. I don't remember the name. There's only one of those that actually has a federal rebate. So we'll have to consider what we're going to do with those particular products when we move forward.

Moving onto the next class is the anti-inflammatory for rheumatoid arthritis. It's mostly just methotrexate products. So the generic products are pretty much preferred and the Trexall auto injector, the brand name is not preferred. The Rasuvo auto injector will be preferred for those that want an auto injector.

Moving on to the next class, which is the analgesics non-steroidal anti-inflammatories we cover multiple strengths of aspirin which are listed first. Multiple strengths of ibuprofen. This is a huge class. It's several pages long. So almost all generics are preferred in this particular class. There are… what were you going to say, April?

April Phillips: [inaudible]

Donna Sullivan: Okay. So there are several slides to look at for this particular class. There is a diclofenac gel product that I believe is preferred, as well. I'm trying to take into account alternatives for opioids for the treatment of pain. Any questions? And just so you know if you're looking at your packet, the slides handout, all of the preferred drugs are the same on each slide. It's the non-preferred drugs that are different. So it starts to make it look like the three slides are just in triplicate, but it's really the non-preferreds that are what's changing from slide to slide. I knew giving you a spreadsheet would make you look at all the data.

Woman: We love data.

Donna Sullivan: I know. Right? Are you ready to move along? You want a few more minutes to look? So to the next slide.

So the leflunomide, ridaura are preferred. Arava is not preferred.

The next slide is the topical analgesics. So we have the lidocaine ointment. There is a lidocaine patch, I believe, that is preferred but it's not listed on here. So there will be that option also for… available.

And then the next slides are the opioids for analgesics. These are actually the long-acting opioids… or the injectables. So just letting you know that the… we're including injectables just because they are in the drug file. So we're also making decisions on whether or not they will be covered under the medical or pharmacy benefit and whether or not PAs will be put on them. So in this instance I think for the most part they are allowed under the pharmacy benefit when they are being used for like home health or something of that nature. So that's why it is in here. So the hydromorphone and the rem… basically the fentanyl generic injectables will be preferred and then the Demerol and methadone injectables will continue to be not preferred.

Nancy Lee: On the Excel sheet it looks like Demerol has a P. Is that gonna change to an N?

Donna Sullivan: It probably just needs to be changed. We're still going through and combing through and making updates. Thanks for pointing that out.

Amber Figueroa: I'm still trying to figure out exactly what this means in the real world as far as what you'd have to do to get something covered. But I'm looking at the lidocaine and there's lidocaine… two lidocaine patches that are covered. Oh, and they both have a Y in prior auth. So that means they need to do a prior auth.

Donna Sullivan: Right. And we have ongoing discussion about whether or not that is going to be on PA or not. So I think we're leaning more towards

not, but we're having just the discussions. The concern with the lidocaine patch is the evidence of its efficacy and then using it off label by using it in areas where, you know, it hasn't been studied. We're just trying to figure out what to do. We're trying to balance the cost of the patches versus allowing it to be used if it was in lieu of an opioid or something of that nature.

Amber Figueroa: So you will save the clinics a lot of money in Tegaderm patches if you cover the lidocaine patch because a lot of the time what we'll do is we will dispense… I mean we will give the patients a patch and tell them to apply the lidocaine and basically make their own lidocaine patch. I didn't say that, but I'm just saying that's what happens in clinical practice a lot.

Donna Sullivan: So we'll save money if we just leave them on PA? Just kidding. So the… so are you saying that you would prefer them not to be on prior authorization?

Amber Figueroa: I think a lot of people just want to try it to see if it works. I think if it wasn't on prior auth and people had a chance to try it…

Donna Sullivan: And if it doesn't work then stop taking it?

Amber Figueroa: They will stop taking it. But I think there are potentially a lot of people that could benefit from it that probably aren't getting it because of the difficulty in doing the prior auth.

Donna Sullivan: Okay. Great. It's going to cost you more money, but I think we might be able to decrease the opioid and just give people a chance to even try it.

Donna Sullivan: Okay.

Jordan Storhaug: I think the other part about that is just the prior auth burden. You can also make the prior auth easy to communicate with what this process is. Then you can do the same thing, but that's very hard to do and so you're kind of left with the option of making it accessible only by not doing the prior auth.

Lisa Chew: Just a quick question about the slide with the lidocaine ointment. There's no utilization data on the capsaicin or was it just…

Donna Sullivan: So if it's not on the spreadsheet there are no claims for it. I don't remember off the top of my head if capsaicin is even covered if it's over-the-counter. I don't think we cover it. So the patients would be paying cash for it. That's a topic to… they are optional so if capsaicin is something that you would want us to consider covering we could take a look at it. We would have to do some budget impact analyses and see if it is going to, you know, adding a new benefit we always have to make sure that we have… it's budgeted for. So it would depend on like what we would expect utilization to be if we were to start covering it.

Lisa Chew: I guess I would like to have that under consideration.

Donna Sullivan: Okay. Okay. So moving on to the next slide, which are the long-acting opioid agonists. So again the fentanyl patches, the morphine ER tablets, oxymorphone ER, tramadol ER are preferred and all of the others are not preferred. That aligns really with how the Washington PDL has been for several years now. And then we are grandfathering people that are on methadone just because that's our current policy. Methadone is kind of… we don't really consider methadone in this class when it's tried and failed. It has its own prior authorization policy and you basically have to try everything other than methadone in order to get approval as a new start. In case you were wondering how methadone was being treated. All of the long-acting opioids, if you remember, we implemented our opioid policy in November so they all require prior authorization or an attestation, not necessarily a prior authorization, but the doctor has to submit that attestation.

Amber Figueroa: On the bottom of the utilization page when there's… the last two are fentanyl patches. They look identical all the way across and one is preferred and one is not. What does that mean?

Donna Sullivan: Um, one is a brand and one is a generic. I think what we decided is this is the 37.5 mg strength.

Amber Figueroa: Oh, the different strengths. Okay.

Donna Sullivan: Yeah. It's $71,000 for 35 claims compared to $60,000 on a 184 claims. Again, that might also be something that needs to be looked into to make sure that that is intentional. But there is one other strength to the fentanyl patches that is much, much more expensive than all of the others and it's not… not necessarily at a dose where you would need it to be preferred.

Next slide is the opioid agonists, the short-acting drugs. Again, there are multiple slides, but essentially the acetaminophen, the generic products are preferred. The oxycodone capsule and solution are not preferred due to cost, but if you needed it and submitted a prior authorization for patients that had difficulty swallowing then it would be approved for that. But we just have it on prior authorization and non-preferred to make sure that the other products are being used first. Again, there's like three slides or more, four slides it looks like for the short-acting agonists. Any questions on this? Okay.

So moving on to the next drug class is the migraine agents. So the triptans. So we are preferring the sumatriptan products as well as the rizatriptan generic products and the naratriptan generic products. Everything else is not preferred and we are not grandfathering this particular class. The majority of the utilization is already… is in those classes. So it is… we're not expecting a lot of disruption.

Next slide is the ergoloid products for migraines and we're making those all not preferred. However, we are going to grandfather everybody in that's already on them. They won't have to change. This will be a forever grandfathering.

David Johnson: Donna, could you clarify. It looks like you have the generic midrin as being non-preferred, but that's actually a DESI drug, I believe. So I don't believe… are we listing DESI drugs at all?

Donna Sullivan: This has… I mean they are being covered right now if they are on this spreadsheet. So I would have to go back and look. I mean if it's not supposed to be covered then we need to go back and look at those to see if there are some corrections that we need to make.

Moving on to the next slide, which is the analgesics, the non-narcotic analgesics. So basically these are the Tylenol combination, butalbital combinations as well. Those go… acetaminophen, the acetaminophen combinations are preferred, the generics and then the others are not preferred. No grandfathering in this class. Any questions?

Moving on to the next class which is the anxiolytics, specifically the benzodiazepines. So alprazolam, chlordiazepoxide, diazepam, lorazepam and oxazepam are preferred. The others that are listed are not preferred.

Man: I have a question.

Donna Sullivan: Go ahead.

Man: Clonazepam is not on this list or is this…

Donna Sullivan: Clonazepam is in the anticonvulsants, I believe.

Man: So say hydroxyzine, clonazepam, so do you… if I'm asked… if I actually prescribe this and I'm asked, "Do they have a seizure disorder" for like gabapentin or clonazepam and if they don't then would it be covered if I'm using… I mean it's nice to have non-benzodiazepine antianxiety meds. They're not great antianxiety meds, but they are wonderful to kind of have for those people that, you know, you can give this to and now I'm being challenged because, you know, they don't have a seizure disorder.

Donna Sullivan: So the klonopin I don't think is on PA. So I don't know why it would be challenged for not having a seizure disorder. This is just how we categorize them. It doesn't mean that they're not in a different class. So like hydroxyzine is in the antiemetic class, I believe. Or it might be in the… I just realized that it doesn't look like we have the slide with the other anxiolytics here. So Buspirone and all of those are going to be here. I think we just omitted the slide probably accidentally and it's not on the spreadsheet. It will be presented next time, but definitely we're [inaudible] the full spectrum of anxiolytics. It's not just these.

Man: I'll wait until next time.

Donna Sullivan: Any questions about the benzodiazepines? Moving forward then with the anti-infective drugs. So these are just the miscellaneous drugs and this is how MediSpend classifies them. I just kind of went with that. So it lumps all together the… a lot of the combination sulfa drugs, as well as the vancomycin, metronidazole. Again, most of these are generic and they are preferred. If there's an M in the preferred status that means it's an injectable and it's covered under the medical benefit.

Moving to the next slide the antimycobacterial agents. So the only one that's not preferred is the myambutol, which is the brand for Ethambutol. Because it is a multi-source brand we're not grandfathering that particular class. And we're going to put a prior authorization on the capastat and the priftin. Questions?

Moving to the next slide then the antibiotics, the cephalosporins, first generations mostly the generics are preferred. The brands are not preferred. We can go to the next slide.

So the second generation antibiotics pretty much the same. If it's a generic it's preferred. The brand name suspensions if there's no generic are preferred.

Alex Park: I'm having trouble keeping up. Can I take us back to the antianxiety benzodiazepines?

Donna Sullivan: Sure.

Alex Park: Can I ask why is it that the generic for the lorazepam tab is… I'm sorry, the brand for the generic… what am I trying to say? The brand for the lorazepam is not preferred, but the brand for the alprazolam is preferred?

Donna Sullivan: So some of the drugs… and sometimes this is… it could be an error. I think that's an error. So sometimes when a drug goes from brand to generic it's marketed under what is called as an authorized generic. So for the sense of CMS it is considered a brand because it's priced as a brand and it's being marketed from a new drug application as opposed to abbreviated new drug application, which is how generic drugs get approved. So it's how the drug referenced company identifies whether a drug is a brand or a generic. Sometimes you'll have a drug with a label name like lorazepam on the third line up and says it is a brand whereas the one right below it says it is a generic. Well, those are both like generics… considered generics. One is… though like a branded generic or it's an authorized generic. I believe the Ativan being preferred is just an error.

Alex Park: The alprazolam being preferred is an error?

Donna Sullivan: Actually that's… yeah. The alprazolam. Let me get on the right page. And then the alprazolam… the ODT is not preferred, the oral tablets are preferred, the Xanax is not preferred and the alprazolam ER is not preferred. So is it the difference between the ODT and the… so the alprazolam, the second line down, again, that's the drug reference table considers that generic product to be a brand because it's being marketed under a new drug application as opposed to being a generic. It's complicated. I should have just gotten rid of this column before I gave this to you. Next time around we'll get rid of some of the columns and try to roll these into smaller lists for you to comb through.

Jordan Storhaug: I think you guys are just going to educate me about this, but I see with the vancomycin most of the use for oral vancomycin has been tablets. That's with my practice and it looks like we're moving to not cover those anymore. And the IESA is moving towards using more oral vancomycin.

Nancy Lee: I think for the treatment of c-diff vancomycin is… are you thinking of like the capsules for c-diff? Liquid is also being used as well now.

Jordan Storhaug: Right now I haven't seen a lot of that, but that's kind of the transition I think that… I think maybe…

David Johnson: Yeah, so the first… it's from a company called [inaudible] Pharmaceuticals and first… compounding kits so the first vanco kit is the preferred vanco product because it is way cheaper than generic vanco capsules.

Nancy Lee: And in terms of the absorption in c-diff I think the oral… not the capsule is maybe better absorbed in patients with c-diff.

[crosstalk]

Nancy Lee: That is correct. Right.

Donna Sullivan: Any other questions?

Jordan Storhaug: I guess with that the suspension… well I guess the suspension is probably… it's not even listed on this. So is it relatively new?

David Johnson: It's been around for a while. I mean, yeah, it's listed just below trimethoprim. I'm sorry, I'm looking at the slides.

Jordan Storhaug: I see that it is there, but…

Donna Sullivan: There's no claims for it if it's not on the spreadsheet. It just means we don't have a claim for it.

Jordan Storhaug: Which means it hasn't been being used.

Donna Sullivan: It's not being used.

Jordan Storhaug: Yeah.

Donna Sullivan: Yeah. But what we're saying is that we'll be…

David Johnson: Molina went to it being preferred as of January. So we… and we're approving it. The new guidelines from a couple of weeks ago is you don't use metro at all. You go straight to vanko. So any requests, at least for us, any request that comes in we're just auto approving it.

Jordan Storhaug: All the doctors I'm working with right now are used to prescribing capsule format for that and so that therefore will then… pharmacies will need to recontact doctors. Is that [inaudible] for those?

Donna Sullivan: Yes.

Jordan Storhaug: It sounds like it's probably an appropriate financial decision to make, but it does sound like this is going to be a transition in prescribing practices that will need to happen.

Donna Sullivan: I agree. It looks like just over 600 patients that were on this and I don't know how many claims that was. But $400,000… they are just very, very expensive, the capsules, and so whatever they are doing to get the guidelines updated…

Jordan Storhaug: I guess if I were in your shoes I guess I'd be expecting that there would be a number of physicians who would be, you know, going, "I can't treat c-diff in patients" and things like that. I mean I don't know what the solution is for that… for getting that information out there, but…

Donna Sullivan: Meaning just to ask them to prescribe the suspension instead of the capsules?

Jordan Storhaug: Yeah. I mean like, yeah. Otherwise I think there would be a number of physicians who think, "Why do I have to do a prior authorization to treat c-diff?"

Donna Sullivan: I don't think it's a prior authorization. I think…

Jordan Storhaug: They don't, but… do they know this? Are they going to know the appropriate next step and are the pharmacies all going to know? That's just a question I have.

Susan Flatebo: I think most of the pharmacies they… when they get a reject code it will tell them suspension is covered or change the suspension and usually then they will contact the provider and…

Donna Sullivan: Just write vancomycin 500 mg or whatever the strength is and then… [laughing]

David Johnson: Even in Washington with therapeutic substitution laws theoretically if you read the law you wouldn't have to call to change it. We're not governed by AB substitution laws. We're governed by therapeutic substitution laws. Granted most pharmacists won't do that, but that's the pharmacists' problem.

Woman: Right. The problem there is pharmacists are governed by corporations in the vast majority of cases and so corporations limit them a lot more than the State of Washington limits them.

Donna Sullivan: Yes.

Woman: And that would be frustrating.

Donna Sullivan: So we can try to make some extra special efforts around this particular topic if you… to make sure that providers know this in case it is a problem, because it is going to be something where it's

an acute issue, not something that you want to have to struggle with trying to figure it out for a day or two.

Jordan Storhaug: My experience is, you know, for simple… it's not even uncommon that I will have written for a generic, but the pharmacy will send the brand, you guys, the insurance company, will reject it and my patient doesn't leave with the medication and I have to call up the pharmacy and say, "Can you run it as a generic?" The system doesn't always work as ideal as [inaudible].

David Johnson: I would recommend they find a new pharmacy.

Woman: 100%.

Man: But they are really nice.

Woman: They are really nice, they just don't give me my stuff.

Man: Right. Doesn't matter if they are dumb.

Donna Sullivan: Okay.

Amber Figueroa: I'm backing up as well. Under antimycobacterial tell me the reasoning behind, if you know, out of all of these things, the reasoning behind having a prior auth for rifabutin. It doesn't look that expensive and it really only has, I think, one indication. It just seems like it might be unnecessary.

Donna Sullivan: Other than we all sat around the table and said it sounded like a good idea, I don't know. Are you recommending we not have it on PA?

Amber Figueroa: Yeah, I don't think we need it.

Donna Sullivan: Okay. I don't remember actually if there is a recommendation that it not be used. So we'll get back to you on that. I know we did this for a reason, because I think we probably had this conversation, but I don't remember exactly why. The other one is

an injectable so that's probably why we put it on PA to make sure that they were trained on how to use it if they are going to get it through the point-of-sale system. But this particular one… I want to make sure that there wasn't a reason other than we decided that there's not a clinical reason to not want people to take this particular drug.

Amber Figueroa: I treat a fair amount of latent TB because I do immigration physicals and I think… it's been a couple years since I treated somebody but that 12-week regimen for latent TB I think it's one of the components of the 12-week regimen. And so for some people when they're not going to be around for very long and time is of the essence sometimes that's really handy to have.

Donna Sullivan: Okay.

Amber Figueroa: I think it's also one of the potential treatments for active TB, but if it's not covered by their insurance that's being monitored by public health. So they would be able to get it for them if they had active TB.

Donna Sullivan: I will definitely look into that. Okay. Are we ready to go on to the cephalosporins? We were about to go to the third generation cephalosporins. Do we need to go back to the first and second?

Amber Figueroa: I don't think so.

Donna Sullivan: So we can move onto the third generation. So basically generics are prefer… the generic cefdinir capsules and suspension are preferred. Ceflixime generic is preferred. The suspension as well as the cefpodoxime tablets and suspension. And the Suprax injection is preferred and available at the pharmacy. Questions?

Amber Figueroa: What's the M?

Donna Sullivan: Medical. That is covered under the medical benefit.

Amber Figueroa: Okay. Thanks.

Donna Sullivan: So it is mostly where you will see injectables or these are piggy-backs it looks like.

And then moving on to the fluoroquinolones. Preferring the ciprofloxacin and the levofloxacin. So all forms of the ciprofloxacin and then the levofloxacin tablets. Questions?

So the next slide is looking at the inhaled aminoglycosides. So we had reviewed these before and we actually… you had made the recommendation to have the Bethkis, Kitabis and Tobi Podhaler as preferred and that the others be non-preferred. These are all tobramycin. It's just different products of tobramycin.

And then on the next slide the Cayston is also preferred with a prior authorization and that basically they have to have the indication to use Cayston and they have tried the tobramycin if the tobramycin was indicated for… or the infection was susceptible to tobramycin.

Moving onto the next slide then are the lincosamides, oxazolidinones and the streptogramins. So clindamycin capsules are preferred as are the clindamycin or the linezolid suspension and the linezolid generic tablets. Any questions on those?

So the next class is the macrolides. So erythromycin generic, azithromycin, clarithromycin generic are preferred. Just things to point out – the erythromycin base is not preferred, but the other generic erthromycins are. The clarithromycin extended release is not preferred and I think those are the only notable things to point out. Dificid is not preferred as well. Questions on those?

So the next slide is the natural penicillins and these are particularly the regular penicillin. So they are all preferred. I think we can move pretty quickly.

The next class is the penicillin combinations. Of note here is the basically generic Augmentin is preferred. The zosyn piperacillin

tazobactam – those are medical drugs so that's what the M is indicating. Nothing really to point out here.

The next slide is the penicillinase-resistant penicillins. So the dicloxacillin is the only oral project and then the rest of them are injectables. So dicloxacillin is preferred and the others are… will be mostly covered under the medical benefit.

The next slide is the sulfonamides. Basically the sulfadiazine is by itself in our drug… go ahead, Amber.

Amber Figueroa: Where's oral amox without [inaudible]?

Donna Sullivan: Um… it is… we just didn't get that slide in there. So there is an amino penicillin class that we will look at next time. I know for sure it's in there. The way we sorted this it just got filtered out, I think, accidentally. The generics are preferred for the most part. We'll talk about that next time.

So the next class are the tetracyclines. So doxycycline hyclate tablets are preferred. The doxycycline hydrochloride… or I'm sorry, the demeclocycline hydrochloride is not preferred. The doxycycline delayed release tablets are not preferred. The generic doxycycline monohydrate capsules are preferred and the difference between… usually the difference between coverage here between a capsule and a tablet is usually one is cheaper than the other, which is what is driving the difference there. Any questions?

So the topical antibiotics we're moving into again mostly over-the-counter products that are preferred. So the bacitracin, gentamicin creams, ointments are preferred. And the mupirocin cream is not preferred, but the mupirocin ointment is preferred. We chose to put the bactroban nasal in this particular class because you could use the topical ointment intranasally if you needed to. Questions?

Okay so the vaginal antibiotics are the [inaudible], the metronidazole and the clindamycin products are preferred. Mostly just the brands are not preferred.

Going to the net class is the anticoagulants. So these are the warfarin products that were not included in the January implementation. So the generic warfarin preferred brands not preferred.

The next slide is the anticoagulants looking at the low molecular weight heparins, which were also not included in the January rollout. The newer anticoagulants so like Xarelto, Eliquis, all of those went preferred in January. So that's why they are not on this list. They are already on the PDL.

Going to the next slide so Dale, this is where your clonazepam comes in. It's the benzodiazepines that are specifically for anticonvulsants. So Onfi is not preferred. We're preferring the clonazepam generic tablets and then the… all of the diazepam rectal products, including the brands are going to be preferred and the reason being is that the generic, I believe, is no longer available or will shortly be out of… so it's gone. And it was actually more expensive than the brand anyway. So all of those products will be preferred.

Moving on to the carbamates. So the felbamate is not preferred, but we're grandfathering. In this particular anything that's going to be changed or not preferred… or from preferred to not preferred we're going to grandfather for obvious reasons.

The next page, the slide… the gaba modulators. Those are all not preferred.

Amber Figueroa: Looking at… I remember when we made that decision that the anticonvulsants should be grandfathered. But looking at this vigabatrin powder pack versus the tab, there's 15 people on the powder pack and it's $1.3 million. I'm wondering if we could ask them to try the tab?

Donna Sullivan: That's the Sabril I think you're looking at?

Amber Figueroa: I don't know. I mean I guess it's not even that much…

Donna Sullivan: Oh, you know what? Normally I would have said… those 15 people, I forget where they are at, sometimes it's… we've done that because they have already been authorized to be on it because it is a multi-source brand.

Amber Figueroa: It looks like it is expensive. All the forms are expensive. It's neither here nor there, but…

Donna Sullivan: We can take a look at that if you… if it's a multi-source brand I feel more comfortable doing it.

David Johnson: I think most, at least for Molina, I think most of those patients are refractory epilepsy kids who can't… or adults who can't swallow and are on a tube or something like that. That's why they are on the powder versus the oral.

Donna Sullivan: Yeah. Most of these are already on prior authorization so they have already been approved to have it, which is one of the reasons why we figured we'd just grandfather. Or if we didn't grandfather it might not matter because they are on PA anyway and it will just go through that process. Any other questions?

So moving on to the hydantoins on the next slide. So the phenytoin… pretty much all of the generics are preferred.

Going to the next slide is just the miscellaneous anticonvulsants. So Vimpat is preferred. The lamotrigine generics are preferred. I need to figure out which direction I'm going here. Some of the lamotrigine, the chewables, are more expensive so they are not preferred. They will be on PA and they will be allowed if a patient can't swallow a tablet. Again, we're grandfathering current users. Just to point out the levetiracetam oral solution is preferred. Trokendi is preferred. Topiramate ER is preferred, but the brand

is not. The generic is. Zonisamide is preferred. Carbamazepine ER is preferred. The gabapentin generics are all preferred. And oxcarbazepine is preferred, as well as the primidone. Again, I think most of the preferred selections really does line up with the… with where the utilization is and then we're just going to grandfather everybody else.

Moving to the next slide is the valproic acid products. So here all the generics are basically preferred. So divalproex sodium is preferred including the extended-release and the 24-hour tablets and also the valproate acid oral solution is preferred.

The next slide is moving on to the antidepressants. So the monoamine oxidase inhibitors are all preferred.

The next slide which is antidepressants other. So the buprenorphine… or I'm sorry, the bupropion generic preferred, the mirtazapine ODT, the [inaudible] tablets are preferred. And then there's the trazadone is preferred. Again, in this particular class we have statute that has refill protection if these were on the Washington PDL. So we're just going to grandfather them. Unless they are a multi-source brand we're not grandfathering those. So that's why there are some zeros and some 99s.

The next class is the antidepressants, the SSRIs. So these all… the antidepressants are already on the Washington PDL so just to let you know that these are aligning with what we currently have as preferred for the Fee-For-Service Program. So looking at the Fluoxetine generic capsules. One difference is the tablets are… some of the tablets are… I'm not sure if this is an error or not. Showing as preferred or not preferred. I'll have to go back and look to see which those are supposed to be. And then the paroxetine tablet is preferred. Mostly the generics are preferred and the brands are not preferred with the exception, I think, of fluvoxamine… we have one of those preferred too. Any questions?

So moving on to the next class is the SNRIs. So venlafaxine capsules, the extended release capsules are preferred, but the tablets are not preferred and that is due to the cost of the tablet is significantly more than the capsules. And then the duloxetine generic will be preferred. And desvenlafaxine will remain not preferred.

And the final slide is the tricyclic antidepressants. So again just mostly generics preferred, brands not preferred. And we're done.

David Johnson: Were we going to change the trimipramine to non-preferred?

Donna Sullivan: I believe so. I think some of the changes that we discussed were not updated in this. So, yes. Any questions?

Lisa Chew: Any questions? That's a lot of work.

Alex Park: Can I take us back to ceflixime? It doesn't look like we have a tablet form that is preferred. Tablet or capsule form that is preferred.

Donna Sullivan: Of the ceflixime?

Alex Park: Yeah. I see the suspension. Is that right? We probably want to have at least one that's…

Donna Sullivan: I'm going to go back to the other slide because we're looking at the utilization versus the actual class. So I believe that the ceflixime, and I'd have to go back and double check. So just because it's not on this spreadsheet does not mean it is not preferred. It's possible… I don't see it listed as not preferred. I just don't… other than the brand, the Suprax, being not preferred, but if there is a generic for Suprax in capsules it is possible we don't have any claims and that's why it is not on the spreadsheet, but I will go back and double check that. I don't remember if it's generically available or not.

David Johnson: No. The generics are gone. There's brand Suprax chewable tablets and brand Suprax 400 mg capsules. The other solid oral dosage generics are off the market. There is generic on some of the suspension, but it is brand only on the chewable tablets and the capsules.

Donna Sullivan: So the question would be are the other two tablet products not suitable alternatives to ceflixime oral?

Alex Park: I think the chew would be fine. It's just they had 10 on preferred status so I thought…

Donna Sullivan: The chewable tablet and the capsule are both brand. And that's why they are not preferred because there's… the cefpodoxime tablets and the cefdinir capsules are preferred and that's what I'm asking if you feel that one of these Suprax needs to be?

Amber Figueroa: In my experience this is how it works. You have somebody who is allergic. So then you look on UpToDate to see what you're supposed to prescribe. They give you this big long list. You pick the first one, send it through and see what happens. When it comes back and it says it's not covered you get back on UpToDate and pick the second one. I mean that's… so… in my experience I would think that having two covered in that class would be sufficient. I mean two of the three are covered plus injectables. So I personally, for my practice, I would think that would be sufficient.

Man: Donna, is this an issue that public health would weigh in on as far as treating SDIs?

Donna Sullivan: Maybe. Or you could argue why somebody could take the liquid, the suspension? So it's not like we're not covering it at all. We're just not covering the capsule.

Man: I can understand the reason.

Donna Sullivan: Yeah.

Petra Eichelsdoerfer: Remembering also that this is a drug that is dosed once-a-day. So the portability for doses later in the day when a person is out and about is less than an issue.

Donna Sullivan: We can look at it. I'll go back and double check the cost too. We don't want to be pushing people to the suspension if it is more expensive when we could be paying for the branded capsule or the tablet. Any other discussion? So you're more than welcome to email me if you have questions, but don't email each other with your questions. If you want something to be brought back next time, if you have questions, you can just let us know if you'd like something to be brought back when you had more time to actually go through this if you feel like going through this in more detail if you have trouble sleeping tonight, maybe. But you're more than welcome to let us know if you have any questions, but I just ask that since you are a board convening you can't do any work outside of an open public meeting so you're not allowed to discuss this amongst yourselves, but you can fire questions to April and I and to Leta and she can pass them along.

Lisa Chew: Thank you, Donna.

Donna Sullivan: You're welcome.

Lisa Chew: Any last questions? I think we are adjourned.