ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

Location of Meeting
Frontier Building, 3601 C Street, Room 890/896

MINUTES OF MEETING
January 22, 2016
8:00 a.m.

Committee Members Present:
Jeffrey Demain, MD, Chair
Marvin Bergeson, MD (telephonic)
Robert Carlson, MD (telephonic)
Vincent Greear, R.Ph. (telephonic)
Jenny Love, MD, Vice Chair
Claudia Phillips, MD
Maggi Rader, CNM (telephonic)
John Riley, PA (telephonic)
Trish White, R.Ph
Ryan Ruggles, PharmD
Diane Liljegren, MD (telephonic)

Committee Members Absent:
John Pappenheim, MD (excused)
Chuck Semling, PharmD (excused)

Others Present:
John McCall, R.Ph., Magellen Management, Clinic Call Center
Erin Narus, PharmD, State of Alaska
Rebecca Wall, PharmD
Jay Butler, MD
Mary Tvenge, Kron Associates

1. Call to Order – Chair

Chair Demain called the meeting to order at 8:00 a.m.

2. Roll Call

A quorum was present. Chair Demain welcomed everyone to the meeting. Dr. Narus explained the new conferencing system and how it should be used. Pressing #0 takes you to the operator, *6 mutes a telephone line, *7 takes the telephone line off mute. She then explained the format of the meeting.

3. Public Comments - Local Public/Health Practitioners

CHERYL said she was a health advocate with Caring Ambassadors, a nationwide health advocacy organization that deals with hepatitis C and liver disease. Because of the November 5, 2015, CMS letter sent to the states, we are meeting with P&T Committees across the country. She wanted to talked about what is was like to have hepatitis C and to work in a research clinic that deals with liver disease. Having a metavir score criteria to be approved for the treatment of hepatitis C is unheard of in the industry. It basically requires patients to have an injury as a result of the disease to qualify for treatment. At no time is hepatitis C safe or not contagious. Receiving treatment does not mean there will be an easy protocol to follow. Patients could have mutations or other issues that impede their ability to respond to the medications. The new drugs are amazing, but some people may have to use the older drugs. She personally had two strains of hepatitis C, 1a and 1b, both of which were successfully treated. She wanted to ensure that other patients with hepatitis C had access to treatment. The cost of treatment needs to be looked at as a systemic issue for liver disease and not just certain types of hepatitis. The cost of treatment is not comprehensive enough and does not include the total cost of treatment or the burden of our families and communities.

Dr. Demain introduced Ryan Ruggles, a new P&T Committee member; Dr. Jay Butler, from the State of Alaska; and John McCall, the new representative for Magellan Management.

4. Re-Review of Anticoagulants (Red Class)

CHRIS CONNER, a representative of Bristol-Myers Squibb, discussed Apixaban (Eliquis). Eliquis is FDA approved for the reduction of risk of stroke or systemic embolism in patients with nonvalvular atrial fibrillation. It is indicated in prophylaxis of DVT, which can lead to PE in patients that have had hip or knee replacement surgery. It is also indicated for the initial treatment or reduction in recurrence of DVT or PE. There is a black box warning with Apixaban, like the other drugs in this class, which points out the increased risk of thromboembolic events for patients that discontinue prematurely and an increased risk of spinal hematoma in patients undergoing spinal anesthesia or spinal puncture. Contraindications include hypersensitivity and patients with active pathologic bleed. It is not recommended in patients with prosthetic heart valves. The most common adverse events are related to bleeding. For complete information on adverse events, contraindications, warning, precautions and dosing, please review the prescribing information. The ARISTOTLE trial and its outcomes were reviewed. Covering Medicaid committees in Alaska, Washington, Idaho and Oregon allows me to see how other states address similar issues. If the intent is to limit or restrict the drugs in this class, consideration should be given to patient management due to the increased risk of thromboembolic events when patients are not adequately bridged. An analysis is available on this issue from the DUR Board in Oregon.

DORIS RIOUX, a representative of Daiichi Sankyo, discussed Edoxaban (Savaysa). Savaysa is a once daily factor Xa inhibitor indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. It should not be used in patients with creatinine clearance greater than 95 milliliters per minute because of an increased risk of stroke, compared to Warfarin. It is also indicated for the treatment of deep vein thrombosis and pulmonary embolism, following five to 10 days of initial therapy with a parental anticoagulant. It is available in doses of 30 and 60 milligrams. Several studies and their outcomes were reviewed. Once-daily Savaysa can provide Medicaid patients with a combination of significantly less major bleeding, versus Warfarin, and a reduced risk of stroke or

systemic embolism for nonvalvular atrial fibrillation. It also provides a treatment option for patients with DVT or PE. It has no mealtime restrictions, convenient once daily dosing, and requires no routine blood monitoring. It is the only once-daily choice with proven superiority over Warfarin relative to major bleeding. For complete information on the use of Savaysa, please see the full prescribing information including boxed warnings, medication guides and other safety information. We request that Savaysa be added to the preferred drug list without restrictions.

BRENT WRIGHT, a representative of Boehringer Ingelheim, discussed Praxbind, the systemic reversal agent for Pradaxa. Praxbind is a humanized monoclonal antibody fragment indicated for patients treated with Pradaxa during emergency surgery and urgent procedures when there is a need to reverse Pradaxa's blood-thinning effects. It is important to note that this indication was approved under accelerated approval. Continued approval of this indication may be contingent on the results of an ongoing case study. Dosing and administration was reviewed. Praxbind only comes in one dose, 5 grams in two separate vials. There are no restrictions for age, renal function or dose of Pradaxa. There are currently no contraindications. Warnings and precautions were reviewed. Pradaxa can be resumed 24 hours after the dose of Praxbind. There is a risk of serious adverse reactions in patients with hereditary fructose intolerance and the risks should be weighed against the benefits. The most common adverse reactions in healthy volunteers were headaches. It should not be used for patients who are pregnant or nursing. Praxbind is the only FDA approved specific reversal agent and shows no other effect on other anticoagulants in the market so it can only be used to reverse the effects of Pradaxa.

DR. MEG QUAN, a representative of Janssen, discussed Rivaroxaban (Xarelto). Based on 2013 DHSS vital statistics for Alaska, cardiovascular disease is the second leading cause of death and strokes are the fifth leading cause of death in the state. This underscores the need for utilization of Xarelto, which was studied in patients with the highest CHAD score and enrolled the greatest number of patients with prior strokes across all NOAC trials in nonvalvular atrial fibrillation. It has shown consistent efficacy and safety profiles for patients with nonvalvular atrial fibrillation across different levels of renal function. It now has a starter pack for VTE treatment for the first 30 days of therapy, which improves medication adherence. Several studies and their outcomes were reviewed. Xarelto has been approved for stroke prevention in nonvalvular atrial fibrillation and VTE prophylaxis following hip or knee surgery since 2011, and the treatment of DVT and PE and reduction in the risk of recurrence since 2012. Xarelto continues to be a safe and effective anticoagulation option for all approved indications. Real world evidence demonstrates consistent safety and efficacy, as well as reduction in length of stay in hospital admissions. It is the only once-daily formulation available in Alaska and studies have shown that adherence rates are consistently higher with once-daily formulations. It is available on the formularies of all major hospitals in Alaska, including the Alaska Native Hospital. We request that Xarelto continue to be included on the preferred drug list and to consider removing the prior authorization to align with the latest guidelines.

Dr. Narus read letters from two local physicians. Dr. Ilona Farr, Alaska Family Medical Care, wrote in support of including Rivaroxaban (Xarelto) on the PDL without restriction, especially for patients who cannot tolerate Coumadin or Warfarin. Dr. Krzysztof Balaban, Alaska Heart and Vascular Institute, wrote in support of Apixaban (Eliquis), which has superior tolerability over the other agents.

Mr. McCall gave the Magellan presentation on Anticoagulants. Anticoagulant therapy is indicated for VTE and atrial fibrillation. The older drugs will still be used. Low molecular weight heparins are the drug of choice for pregnancy, cancer patients, and those with liver disease. Warfarin is the drug of

choice for patients with mechanical heart valves. The 9th American College of Chest Physicians Evidence-Based Clinical Practice Guidelines were reviewed. These drugs are renally cleared. Several of the drugs as dosed once a day. The new drug in the class, Edoxaban, has some drug interactions and the dosage has to be adjusted with Azithromycin, Clarithromycin, Erythromycin, oral Itraconazole or oral Ketoconazole. In addition, dosing adjustments must be made for patients with healthy creatinine clearance. In November 2015, there were 299 claims with 86 percent for the preferred agents. At the last review, a motion for therapeutic alternatives to include one oral agent, one injectable and Warfarin passed unanimously.

In response to Dr. Demain, Mr. McCall said there were procedures for taking patients off these medications, but there were ongoing problems. There is no current study addressing this issue.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE ONE ORAL AGENT, ONE INJECTABLE AGENT AND WARFARIN. SECONDED BY DR. BERGESON.

The committee discussed whether Pradaxa should be included on the PDL since it was the only drug with a reversal agent. Dr. Liljegren felt Pradaxa should be included on the PDL. When working in an isolated area, it was very important to be able to reverse an agent's action.

DR. PHILLIPS AMENDED THE MOTION THAT THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE ORAL NON-WARFARIN AGENT, TO INCLUDE PRADAXA; AT LEAST ONE INJECTABLE AGENT; AND WARFARIN. THE SECOND CONCURRED. THE MOTION PASSED UNANIMOUSLY.

5. Re-Review of Lipotropics, Other (Red Category)

DR. SYLVIA CHURCHILL, a representative of Amgen, discussed Evolocumab (Repatha). Repatha is a human monoclonal antibody that inhibits PCSK9, which is a protein that reduces the liver's ability to remove LDL or bad cholesterol from the blood. This is a new class of cholesterol lowering agents. The mechanism of action for Repatha differs from that of the statin drugs. It is not to be used in place of statin drugs, but is indicated in addition to statins for those patients that are already on maximally tolerated statin dosages yet still require additional lowering of their LDL levels. Repatha leads to significant decreases in LDL cholesterol levels when added to maximal statin therapy. Several trials and their outcomes were reviewed. It is indicated for patients with clinical ASCVD, which means that they have already experienced a major atherosclerotic event and we are trying to prevent another one; those with HeFH, which is an inherited conditions where patients have twice the risk of having a major atherosclerotic event; and those with HoFH, an inherited genetic condition that is rare but includes very high risk patients. It is the only PCSK9 inhibitor that has the indication for HoFH. For all three of these indications, Repatha is indicated in addition to maximally tolerated statin therapy for patients who still need lowering of their LDL levels. These agents need to be stored in a refrigerator, but it is the only PCSK9 inhibitor that has shown stability at room temperature for up to 30 days, as well as temperatures up to 104 degrees and down to -22 degrees. It is a subcutaneous injection every two weeks or once a month. It comes in pre-filled auto injectors that include safety features.

In response to Dr. Demain, Dr. Churchill said the guidelines have changed over the years. Where you used to say an LDL level should be below 100 or 70 depending on the diagnosis, we now want to

decrease that level by at least 50 percent. Repatha is very effective at decreasing LDL levels, but may not be the appropriate agent for patients who only need a slight decrease.

In response to Dr. Carlson, Dr. Churchill said there currently was no data on the outcomes of Repatha on cardiovascular, morbidity and mortality, but data from ongoing studies involving over 27,000 patients should be available by the end of the year.

Dr. McCall gave the Magellan presentation on Lipotropics, Other. In 2013, the ACCAH made major changes to the guidelines. Patients were put into high risk or moderate risk categories. As a result, more patients were prescribed statins, because they were beneficial regardless of how much the patient's cholesterol was lowered. The American Diabetes Association agreed with this approach and more people were started on higher doses of statins. They did not find any proof that the other drugs helped versus the related adverse effects. An exception was the IMPROVE IT trial for Zetia, which showed fewer cardiovascular events with Zetia. However, the drugs in class are still used, especially to lower triglycerides. The PCSK9 inhibitors, Praluent and Repatha, came into the market and appear to decrease cholesterol by 40 to 60 percent from baseline. Repatha is the only drug in the class with indications for homozygous hypercholesterolemia. Since November 2015, there were 284 claims with 91 percent being preferred agents. At the last review, a motion for therapeutic alternatives to include one drug from each subclass passed unanimously.

Dr. Demain noted that the anticoagulants, which were reviewed earlier in the meeting, no longer required prior authorization and now has open access.

Break from 8:54 a.m. to 9:00 a.m. after experiencing problems with telephonic participants not muting their telephones while having other conversations.

Dr. Demain called the meeting back at to order at 9:00 a.m. and did a roll call vote.

The committee continued discussing the Lipotropics, Other class. Dr. Liljegren did not feel it was necessary to include one drugs from each subgroup, but the bile acid sequestrants, fibric acids and cholesterol absorption inhibitors should be included, and the drugs within those subgroups were therapeutic alternatives.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE BILE ACID SEQUESTRANT, ONE CHOLESTEROL ABSORPTION INHIBITOR, AND ONE FIBRIC ACID.

In response to Dr. Phillips, Dr. Liljegren said there was no benefit in excluding any of the classes, but the other drugs were not very good. Dr. Demain said the medically necessary clause could always be used to prescribe non-preferred agents. Dr. Love noted that Niacin ER was 10 percent of the utilization and the motion could cause it to be removed from the PDL. She felt a broader motion would allow a larger pool of resources.

THE MOTION FAILED DUE TO LACK OF A SECOND.

DR. LOVE MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE ONE DRUG FROM EACH SUBCLASS. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

6. Re-Review of Platelet Aggregation Inhibitors (Red Category)

JEANNIE KENYON, a representative of AstraZeneca, discussed Ticagrelor (Brilinta). In September 2015, the FDA approved a new indication for Brilinta, which led to a label change. Brilinta is indicated to reduce the rate of CV death, MI, and stroke in patients with ACS or a history of MI. For at least the first 12 months following ASC, Brilinta is superior to Clopidogrel. Brilinta also reduces the rate of stent thrombosis in patients who have been stinted for treatment of ACS. This new indication was based on a study published in the New England Journal of Medicine in May 2015. The study and its outcomes were reviewed. There is a boxed warning on the increased risk of bleeding and reduced efficacy with maintenance doses of aspirin of greater than 100 milligrams.

Mr. McCall gave the Magellan presentation on Platelet Aggregation Inhibitors. CV deaths have decreased by 31 percent from 2000 to 2011. Anti-platelet drugs are the drugs of choice for the prevention and treatment of arterial thrombosis, MI, stroke, and transient ischemic attacks. For patients with a genetic disposition to poor metabolism, Clopidogrel (Plavix) has an issue related the enzyme CYP2C19 that makes the drug less effective. There are drug interactions with proton pump inhibitors. A new drug on the marketplace is Durlaza. Durlaza should not be taken within two hours before or after consuming alcohol, and non-steroidal anti-inflammatories should be avoided. In November 2015, there were 231 claims with 89.5 percent being preferred agents. At the last review, a motion for therapeutic alternatives to include at least Clopidogrel passed unanimously.

In response to Dr. Demain, Mr. McCall said both Brilinta and Clopidogrel were used in conjunction with aspirin.

DR. (UNIDENTIFIED) MOVED THE AGENTS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST CLOPIDOGREL. SECONDED BY DR. RILEY. THE MOTION PASSED UNANIMOUSLY.

7. Re-Review of Cytokine CAM Inhibitors (Red Class)

DR. MARY KEMHUS, a representative of Novartis, discussed Secukinumab (Cosentyx). Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis. As of last week, it was also indicated for active forms of ankylosing spondylitis and psoriatic arthritis. Cosentyx's mechanism of action binds the IL-17A and inhibits its interaction with the IL-17 receptor. This pathway is important, because IL-17 is found in large concentrations in the skin and joints of patients with psoriasis, psoriatic arthritis, and ankylosing spondylitis. There are currently no other approved therapies that work via this mechanism. Several trials and their outcomes were reviewed. Cosentyx has a consistent and well-tolerated safety profile. Higher rates of Candida were observed when compared with placebo, which is an expected side effect from a mechanism that works on the IL-17 pathway. We request that Cosentyx be included on the PDL.

DR. MARGARET ULLMAN, a representative of Abbvie, discussed Adalimumab (Humira). Humira is now indicated for the treatment of patients with moderate to severe hidradenitis suppurativa (HS).

HS is a painful, chronic, relapsing, debilitating inflammatory skin disease characterized by painful, inflamed nodules that can progress to abscesses, sinus tracts, and scaring. The estimated prevalence of confirmed HS is 127.8 patients per 100,000 in the United States, of which an estimated 40 percent are classified as moderate to severe. The efficacy and safety of Humira in patients with moderate to severe HS was studied in 633 subjects in two trials. Both trials and their outcomes were reviewed. Humira is currently the only FDA-approved treatment for HS. The dosing regimen for Humira was reviewed. Humira has proven efficacy, a well-established safety profile, and maintenance dosing across a wide range of indications. We asked that the committee maintain the preferred status of Humira on the PDL.

In response to Dr. Demain, Dr. Ullman said she did not believe the dosing interval could be widened after control was achieved. A study looking at four-week dosing, two-week dosing, and weekly dosing found that patients responded better on weekly dosing and had both improved rapid responses and better overall outcomes.

DR. JASON ALM, a representative of Celgene, discussed Apremilast (Otezla). Otezla is approved for the treatment of psoriasis and psoriatic arthritis. Apremilast is a small molecule that inhibits phosphodiesterase 4 (PDE4). It is believed to work intracellularly on various immune cells to modulate the release of various cytokines. Several trials demonstrating the safety and efficacy of Apremilast were reviewed. The label includes three warnings and precautions: weight loss, drug interactions, and depression. Recently published treatment recommendations by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis covered six domains of psoriasis and psoriatic arthritis. Apremilast has received recommendations in five of those categories, which were reviewed.

DR. CLARIBEL TAN provided a recommendation based on her clinical experience with Xeljanz. She felt it was a very effective treatment for rheumatoid arthritis. It comes in a tablet form, which makes it convenient, increases compliance, and is easy to mail to rural areas.

DR. MARK JENSON, a representative of Pfizer, discussed Tofacitinib (Xeljanz). Agents used to treat rheumatoid arthritis have significantly expended over the past several years from a single mechanism of action to many different drugs classes with different mechanisms of actions. For example, the 2015 Rheumatoid Arthritis Treatment Guidelines incorporate these advancements in therapy in its recommendations so patients who fail Methotrexate can go to agents other than anti-TNF products. Xeljanz is a non-biologic, small-molecule, orally administered tablet, which is different from the traditional agents. It is approved for the treatment of moderate to severe rheumatoid arthritis in adults who have an inadequate response or intolerance to Methotrexate. It is indicated at a dose of 5 milligrams, twice a day. It may be administered as monotherapy or in combination with Methotrexate or other non-biologic disease modifying drugs. It offers a unique mechanism of action and has the convenience of being administered orally, thus avoiding injections or infusions. Xeljanz does not require refrigeration or complicated injection teaching regimens. Several trials on the safety and efficacy of Xeljanz were reviewed. Xeljanz would be a useful option as monotherapy or in combination with other non-biologic disease modifying drugs for those patients who cannot tolerate Methotrexate or biologic-based therapies due to its unique mechanism of action, its established safety and efficacy profile, and its availability in an oral form.

In response to Dr. Demain, Dr. Jenson said Xeljanz was approved for patients who failed or could not tolerate Methotrexate. There was a robust phase-three trial done, but it was conducted after the package

was submitted to the FDA and was not included in the label. However, the phase-three study was published in the Journal of Medicine.

Mr. McCall gave the Magellan presentation on Cytokine CAM Inhibitors. Cytokine CAM antagonists and related agents treat rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, and Crohn's disease. In rheumatoid arthritis, you start with agents like Methotrexate. If that does not work, you consider the biological agents. In 2015, the Rheumatology Guidelines said that if a patient fails a TNF inhibitor then the recommendation is to move to a non-TNF biological drug. In November 2015, the utilization was 92 percent for preferred agents. He was unsure of last year's motion.

In response to Dr. Demain, Dr. Narus explained that the market baskets were designed by Magellan and based on how the drugs were bid against each other.

The committee discussed the Cytokine CAM Inhibitors. Dr. Demain did not feel some of the drugs should be included on this list. Dr. Narus said those drugs could be classified separately on the PDL, but that would not change how they were bid against each other. Dr. Demain said the anti-interleukin 1 alphas should not be considered within this group and Magellan would be asked to reevaluate them and place them in different classes. Dr. Liljegren felt the motion should include at least one pediatric medication, as well as one that treats arthritis conditions, one that treats psoriasis, and one that treats inflammatory valve disease. Dr. Demain said there now was an oral option in this class.

DR. LILJEGREN MOVED THAT THE DRUGS IN THE CLASS WERE THERAPEUTIC EQUIVALENTS TO INCLUDE AT LEAST ONE FORMULATION FOR PEDIATRICS, ONE FOR ARTHRITIS, ONE FOR PSORIASIS, AND ONE FOR INFLAMMATORY BOWEL DISEASE. SECONDED BY DR. PHILLIPS.

In response to Dr. Demain, Dr. Narus said there have been periodic reports of medications arriving frozen when shipped to remote areas where there were delays in shipments.

THE MOTION PASSED UNANIMOUSLY.

8. Re-Review of Angiotensin Modulators - Angiotensin II Receptor Blockers (Red Class)

There were no public testimonies.

Mr. McCall gave the Magellan presentation on Angiotensin Modulators - Angiotensin II Receptor Blockers. Comparative trials have been conducted between ARBs for the management of hypertension. According to prescribing information, all ARB lower blood pressure to a similar degree. ARBs, like the ACE inhibitors, have extensive data showing renal protective benefits in hypertensive diabetic patients, as well as benefits for cardiac failure patients, those at risk, and prevention. ARBs are also recommended in patients unable to tolerate ACE inhibitors.

DR. MARY KEMHUS, a representative of Novartis, discussed Sacubitril/Valsartan (Entresto). Entresto is a combination of Sacubitril and Valsartan. It is indicated to reduce the risk of cardiovascular death and hospitalization for patients with heart failure and reduced ejection fraction. The first key point is the unmet needs in heart failure management. Despite current treatment options,

mortality rates are high and approximately 50 percent of patients will die within five years of heart failure hospitalization. A clinical trial and its outcomes on Entresto were reviewed. The second key point is the economic value of Entresto. Mortality rates are high, but hospitalization and re-hospitalization rates are a concern in this population. About 80 percent of heart failure patients are hospitalized at least twice a year. In the PARADIGM-HF trial, Entresto reduced the risk of heart failure hospitalization by 21 percent. Entresto safety and efficacy profiles were reviewed.

In response to Dr. Demain, Dr. Kemhus said Entresto was not indicated for hypertension, but only heart failure and reduced ejection fraction. Although there is some published information on the indication of hypertension, it did not make sense for us to enter the crowded marketplace. Mr. McCall pointed out that when a patient was switched from an ACE inhibitor to Entresto, there should be a 36-hour waiting period before starting Entresto.

Mr. McCall continued the Magellan presentation on Angiotensin Modulators - Angiotensin II Receptor Blockers. Adverse reactions with ACE inhibitors include acute kidney and hypokalemia. ACE inhibitors and ARBs should not be combined. At the last review, a motion for therapeutic alternatives to include at least one drug from each subgroup passed unanimously.

The committee discussed the Angiotensin Modulators - Angiotensin II Receptor Blockers. Dr. Narus explained how the drugs in the class were grouped by Magellan. Dr. Liljegren said that several years ago the committee agreed that if each part of a combination were approved separately then the combination would automatically be approved. Dr. Demain said the other part of that agreement was as long as it was not financially cost prohibitive. Dr. Narus said specific guidance from the committee should be included in the motion so it would be documented. Dr. Phillips asked if Entresto could be managed with the medical necessity clause and/or a prior authorization requirement. Dr. Love noted the new subgroup was indicated for congestive heart failure, not hypertension management, and we want to ensure that the drug is being used correctly so it is not a therapeutic alternative. The committee discussed the definition of therapeutic alternatives. Dr. Narus said the class could be divided or a detailed motion could be made. In response to Dr. Love, Dr. Narus reviewed the prior authorization process. Entresto currently requires a prior authorization because it is on the interim prior authorization list. Entresto is a class one drug, which requires the failure of another drug that treats the labeled indication. The committee could also recommend that the DUR Committee review Entresto and determine if there should be additional clinical criteria assigned to it. Dr. Phillips questioned if Entresto was listed as a therapeutic alternative, to include an agent that treated hypertension as well as congestive heart failure, if the PDL would be built to ensure that there was a product within this class that had an indication for congestive heart failure. The committee discussed a proposed motion.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE DRUG FOR HYPERTENSION AND ONE FOR CONGESTIVE HEART FAILURE. SECONDED BY DR. RUGGLES. THE MOTION PASSED UNANIMOUSLY.

9. Re-review of Angiotensin Modulators - Angiotensin Modulator Combinations (Red Class)

There were no public testimonies.

Mr. McCall gave the Magellan presentation on Angiotensin Modulators - Angiotensin Modulator Combinations. All of the agents in the class are similar. Prestalia, a combination of Amlodipine and Perindopril, is new to the class. It is calcium channel blocker and an ACE inhibitor. It is indicated for the treatment of hypertension in patients not adequately controlled on monotherapy. The potential drug interactions were reviewed. The most common adverse events were headaches and dizziness. It is a Pregnancy Category D. In November 2015, there were 21 claims with 86 percent being preferred agents. At the last review, a motion was to include one drug from each subgroup passed unanimously.

The committee discussed the Angiotensin Modulators - Angiotensin Modulator Combinations. It was noted that the class had changed since the last review. Dr. Demain said combination agents were used when a single again failed.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. RUGGLES. THE MOTION PASSED UNANIMOUSLY.

10. Re-review of IBS - Gastrointestinal Motility Chronic (Red Class)

KAREN CAMPBELL, a representative of Allegan, discussed Eluxadoline (Viberzi), a mu-opioid receptor agonist indicated in adults for the treatment of irritable bowel syndrome with diarrhea (IBS-D). IBS-D is considered the most debilitating of all IBS conditions. Its etiology is still not well understood, but most experts agree that it is multi-factorial and varies from patient to patient. Prior to the approval of Eluxadoline, IBS-D treatment options were limited to mostly non-FDA agents in short-term use due to tolerability issues and side effects. In 2014, a systematic review of the evidence in agents used in IBS-D was done. There are currently two other agents approved for IBS-D, Lotronex (for women not responsive to conventional treatment) and Rifaximin (a non-absorbable antibiotic that was already on the market). Eluxadoline received FDA fast-track review and approval for the treatment of a serious condition with unmet medical needs. Its unique mechanism of action targets the two core symptoms of IBS-D, abdominal pain and diarrhea, regardless of its etiology. It is a mu- and kappa-opiate receptor agonist that slows intestinal motility and reduces visceral pain, but it is also a delta-opiate receptor antagonist that modulates the mu agonist by reducing the risk of constipation and enhancing analgesic activity by reducing tolerance. Several trials and their outcomes were reviewed. We respectfully request that Eluxadoline be available to patients with IBS-D.

DR. RANDY LEGG, a representative of AstraZeneca, discussed Movantik (Naloxegol). It is the only FDA-approved oral peripherally-acting mu-opioid receptor antagonist for the treatment of opioid-induced constipation (OIC) in adult patients with chronic, non-cancer pain. It was approved in the U.S. in September of 2014. Opioids work by binding to the mu-receptors in the brain and other parts of the central nervous system (CNS). They also bind to mu-receptors in the GI tract, which may result in a unique form of constipation. Patients with constipation following opioid prescriptions have significantly higher health care resource utilization and costs compared to those taking opioids without this constipation. The mechanism of action of Movantik was reviewed. Several trials and their outcomes were reviewed. The most common adverse events are abdominal pain, diarrhea, nausea, and possible opioid withdrawal. The package insert is available for review. We respectfully request that Movantik be added to the PDL.

Dr. Phillips left the meeting.

Mr. McCall gave the Magellan presentation on IBS - Gastrointestinal Motility Chronic. Chronic idiopathic constipation is diagnosed if there are less than three spontaneous bowel movements per week with symptoms occurring for six months or more. Irritable bowel syndrome (IBS) is a chronic condition without a cure. IBS occurs in about 15 percent of the population and is more common in women. The symptoms alternate between constipation and diarrhea. Opioid-induced constipation is a common adverse effect of opioid therapy. There is a variety of medications on the PDL. Alosetron addresses IBS and diarrhea. Linaclotide addresses constipation. Lubiprostone addresses constipation and IBS. Methylnaltrexone addresses opioid-induced constipation. The new agents are Movantik and Viberzi. Warnings for Movantik include GI perforation, opioid-withdrawal syndrome, and abdominal pain. Dosages should be decreased if there is renal impairment. Viberzi is a schedule 4 drug that is indicated for IBS with diarrhea. At the last review, a motion for class effect passed unanimously.

Dr. Demain noted there were two categories: treatment of IBS with diarrhea and treatment of IBS with constipation. Dr. Narus said there were also agents that treated opioid-induced constipation.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE FORMULATION FOR DIARRHEA AND ONE FOR CONSTIPATION DRUG. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

Break from 10:29 a.m. to 10:42 a.m.

11. Re-Review Ulcerative Colitis Agents (Red Class)

There were no public testimonies.

Mr. McCall gave the Magellan presentation on Ulcerative Colitis Agents. Most of the drugs in the class are formulations of Mesalamine. The new drug is Budesonide rectal foam (Uceris), which has been approved for mild to moderate active distal ulcerative colitis. In November 2015, there were 54 claims with 72 percent being preferred agents. At the last review, a motion for therapeutic alternatives to include at least one short-released, one long-released and one rectal formulation passed unanimously.

The committee discussed the Ulcerative Colitis Agents. In response to Dr. Demain, Mr. McCall said the Budesonide rectal foam was applied topically and had limited absorption, which was not a major concern. Dr. Liljegren felt the Budesonide oral formulation should be included in this class as it was very useful and different from the other medications. Dr. Narus explained that the Budesonide oral formulation was in the corticosteroid class and was indicated for Crohn’s Disease. Uceris is available in both a foam and tablet formulation and both are part of this class. Dr. Liljegren felt the oral formulation of Budesonide be included in the motion as it was unique and useful.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE LONG-ACTING, ONE SHORT-ACTING, ONE ORAL BUDESONIDE, AND ONE RECTAL PREPARATION.

In response to Dr. Love, Dr. Narus said Uceris did not have a generic equivalent so the motion would include the brand Uceris as the oral Budesonide. Dr. Demain asked if a patient needed to fail on Mesalamine before being prescribed Uceris. Dr. Narus said the motion could include a request for the DUR Committee to review Uceris for clinical criteria associated with its utilization. The committee discussed if Uceris should be a preferred agent or prescribed utilizing the medically necessary clause.

SECONDED BY DR. RADER. THE MOTION WAS A TIE WITH FOUR MEMBERS APPROVING THE MOTION AND FOUR AGAINST.

The committee further discussed the Ulcerative Colitis Agents. Dr. Ruggles felt specifically including Uceris was a disadvantage. Dr. Narus explained that if Uceris were a preferred drug with no clinical criteria, there would be open access to the drug. If the DUR Committee felt that it needed to review Uceris, they could do that. Dr. Liljegren said she would be dismayed if physicians prescribed Uceris for anything other than its indications.

DR. LOVE MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE SHORT-RELEASED, ONE LONG-RELEASED AND ONE RECTAL PREPARATION. SECONDED BY DR. CARLSON. THE MOTION PASSED WITH ONE OPPOSED.

12. Re-Review of Immunosuppressants (Red Class)

There were no public testimonies.

Mr. McCall gave the Magellan presentation on Immunosuppressants. Immunosuppressants are primarily used for organ transplant patients, but Azathioprine and Cyclosporine are approved for the treatment of rheumatoid arthritis and Cyclosporine is approved for the treatment of plaque psoriasis. Tacrolimus has a new long-acting formulation, Envarsus XR, which was reviewed. In November 2015, there were 21 claims with 77 percent being preferred agents. At the last review, a motion for therapeutic alternatives passed unanimously.

Dr. Demain said this category would be driven by the location and protocol of the transplant.

DR. LOVE MOVED A CLASS EFFECT. SECONDED BY DR. RUGGLES. THE MOTION PASSED UNANIMOUSLY.

13. Re-Review of Hepatitis B Agents (Red Class)

There were no public testimonies.

Mr. McCall gave the Magellan presentation on Hepatitis B Agents. Rates of hepatitis B have decreased now that there is a vaccine. Chronic HBV infection occurs in 5 to 10 percent of individuals with acute HBV infection. Lamivudine can be used for short-term treatment when patients are on steroids, are having a procedure, or preceding chemotherapy. The World Health Organization said their preference is Baraclude and (indiscernible). In November 2015, there were three claims.

DR. RUGGLES MOVED A CLASS EFFECT. SECONDED BY DR. LOVE. THE MOTION PASSED UNANIMOUSLY.

14. Re-Review of Hepatitis C Agents (Red Class)

DR. BRIDGET HERNANDEZ, a representative of Bristol Myers Squibb, discussed Daclatasvir (Daklinza). Daklinza is approved for genotype 3 hepatitis injections. It is used in combination with Sofosbuvir for 12 weeks. This combination provides an all-oral, interferon-free option, a shorter duration of therapy for the majority of patients with potential acquisition cost savings compared with the only other indicated regimen. Current estimates are that genotype 3 prevalence is about 13 percent in the United States. However, genotype 3 has emerged as the most challenging to treat and is associated with an accelerated rate of fibrosis and cirrhosis when compared to genotype 1. Patients with genotype 3 are at a 31 percent higher risk of developing cirrhosis and an 80 percent higher risk of developing hepatocellular carcinoma compared to genotype 1. Several studies and their outcomes were reviewed. There is a limitation of use in our label to raise awareness of the reduced SVR that was seen in patients with cirrhosis that were treated for 12 weeks. It is important to note that this is not a contraindication. Additional information on use of this regimen in patients with cirrhosis has been evaluated in our study, as well as real-world data from European and French Compassionate Use Programs. Daklinza is contraindicated for co-administration with strong inducers of CYP 3A4. For complete prescribing information, please consult the package inserts. The AASLD Guidelines have been updated and recommend the use of Daklinza and Sofosbuvir for patients with genotype 3 infections. We request that Daklinza be included on the PDL.

In response to Dr. Demain, Dr. Hernandez said Daklinza was approved for 12 weeks of therapy. The label suggests that the optimal duration of therapy for patients with cirrhosis has not yet been determined, which is why an additional study was done.

DR. MARGARET ULLMAN, a representative of Abbvie, discussed Technivie. Technivie, in combination with Ribavirin for 12 weeks, is approved for the treatment of patients with genotype 4 chronic hepatitis C infection without cirrhosis. It is contraindicated in patients with moderate to severe hepatic impairment as Child-Pugh B and C. It may also be considered for use without Ribavirin in treatment naïve patients who cannot tolerate Ribavirin. Technivie, with and without Ribavirin, was studied in 135 genotype 4 patients in a clinical trial, which was reviewed. The updated labels for Viekira Pak and Technivie, which were approved by the FDA in October of 2015, were reviewed. The previous label did not recommend treatment in Child-Pugh B, and Viekira Pak was contraindicated in Child-Pugh C. The updated label now aligns with your current PA criteria, which excludes patients with Child-Pugh B or C. Viekira Pak and Technivie are now contraindicated in patients with Child-Pugh B and C due to a risk of potential toxicity. The updated label also states that the health care professional should assess for laboratory and/or clinical evidence of hepatic decompensation. Viekira Pak remains indicated for compensated cirrhotic patients with Child-Pugh A. We request that Viekira Pak be maintained on the PDL and Technivie be added to the PDL for patients with HCV.

Mr. McCall gave the Magellan presentation on Hepatitis C Agents. We are following the AASLD liver disease guidelines. The new drugs on the marketplace have changed everything, because all of a sudden, we can treat 90 to 99 percent of patients, but the challenge is the cost. He suggested taking this to the DUR Committee.

The committee discussed the Hepatitis C Agents. Dr. Narus said a vote could be done through the P&T Committee. Some of the products require combination use and there are a few new products. The preferred status is based on the criteria voted on by the DUR Committee, but it is in alignment with the P&T Committee's motion last year of a class effect. Mr. McCall said Magellan closely followed the AASLD Guidelines. Dr. Demain suggested a motion of a class effect to include an appropriate and approved therapy for each genotype and let Magellan work it out.

DR. RUGGLES MOVED A CLASS EFFECT TO INCLUDE AN APPROPRIATE AND APPROVED AGENT FOR EACH GENOTYPE OF HEPATITIS C. SECONDED BY DR. CARLSON. THE MOTION PASSED UNANIMOUSLY.

15. Re-Review of Hypoglycemics Insulins (Red Class)

DR. TODD PAULSON, a representative of Novo Nordisk, discussed Tresiba. Tresiba is a long-acting basal insulin analog. It is indicated for adults with diabetes mellitus. It is the first new molecule in this class in the last 10 years. The mechanism of action of Tresiba was reviewed. It has a half-life of 25 hours, a duration of action of at least 42 hours, and a low glycemic viability of 20 percent. Several studies and their outcomes were reviewed. Tresiba is the only insulin that has an indication to be used at any time of the day whereas other insulins have to be used at the same time every day. Tresiba comes in U-100 and U-200 doses in a flex-touch pen, which that demonstrated stability for up to two months and exceeds all other insulins in the marketplace. The most common side effect is hypoglycemia. It is not indicated for patients with ketoacidosis. The pens should not be shared. Please refer the prescribing information for the other safety information. We request that Tresiba be included on the PDL.

Mr. McCall the Magellan presentation on Hypoglycemics Insulins. There are several different kinds of insulin. Their slight differences are related to how long they act. There is rapidly acting insulin, long-acting insulin, and ultra long-acting insulin. Afrezza, an inhaled powder insulin, is a short-acting insulin. It comes in cartridges of specific doses. Patients with respiratory issues or smokers should not use Afrezza. In November 2015, 81 percent of the prescriptions were for preferred products. The long-acting insulins all come in pens so there is no risk of breaking vials or incorrect dosages. At the last review, a motion for class effect to include at least one formulation from the long-acting, to include a pen delivery system; one from the rapid-acting, to include a pen delivery system; insulin mix; insulin 70/30; insulin N; and insulin subgroups; and preferentially including Lantus passed unanimously.

The committee discussed the Hypoglycemics Insulins. Dr. Love said at the last review, the committee discussed whether to include the pen preparations because of their cost prohibitive nature. Looking at the utilization, the pens are being utilized more than anything else is, which could encourage better compliance, treatment and outcomes. In response to Dr. Demain, Dr. Narus said consideration would be given to the fact that the three medical centers in Anchorage have a protocol for diabetics that patients are prescribed the same medications that were used during their stay at the hospital. The committee discussed the availability of inhaled insulin. Insulin is allergenic and it did not seem like a good idea for patients to inhale it into their lungs. Mr. McCall said bronchospasm was listed as an increased risk for inhaled insulin. Dr. Ruggles said inhaled insulin had been available in the past, but was removed from the marketplace. In response to Dr. Butler, Mr. McCall said inhaled insulins were contraindicated for patients who smoked. Dr. Demain recommended excluding inhaled insulins from the PDL.

DR. LOVE MOVED A CLASS EFFECT, TO INCLUDE AT LEAST ONE FORMULATION FROM THE LONG-ACTING, TO INCLUDE A PEN DELIVERY SYSTEM; ONE FROM THE RAPID-ACTING, TO INCLUDE A PEN DELIVERY SYSTEMS; INSULIN MIX; INSULIN 70/30; INSULIN N; INSULIN SUBGROUPS; AND PREFERENTIALLY INCLUDING LANTUS. SECONDED BY DR. CARLSON. THE MOTION PASSED UNANIMOUSLY.

16. Re-Review of Angiotensin Modulators - ACE and Renin Inhibitors (Green Class)

Mr. McCall gave the Magellan presentation on Angiotensin Modulators - ACE and Renin Inhibitors. Studies have found that ACE inhibitors appear to be equally effective. Tekturna is a renin inhibitor. At the last review, a motion for class effect passed unanimously.

Dr. Demain noted that some of the drugs in this class were pediatric approved and some were not. We are seeing more children with hypertension due to an increase in obesity.

DR. RUGGLES MOVED A CLASS EFFECT, TO INCLUDE AT LEAST ONE PEDIATRIC FORMULATION. SECONDED BY DR. LOVE. THE MOTION PASSED UNANIMOUSLY.

17. Re-Review of Antibiotic, Vaginal (Green Class)

Mr. McCall gave the Magellan presentation on Antibiotic, Vaginal. According to the 2015 CDC Treatment Guidelines, the recommended regimens for the treatment of bacterial vaginosis in non-pregnant women include oral Metronidazole, Metronidazole gel, and Clindamycin cream. In November 2015, 81 percent of the claims were for non-preferred agents. At the last review, a motion for therapeutic alternatives passed unanimously.

The Committee discussed the utilization, which was 81 percent for non-preferred agents. Dr. Narus said that sometimes brand-name products were less expensive than generic ones. It made sense that the practitioners would prescribe the generics. There is no advantage to having the generic in the preferred positions, because there would be no additional rebates. This might be an educational issue on the rationale of selecting a branded product over a generic product in this situation.

DR. LOVE MOVED A CLASS EFFECT. SECONDED BY DR. LILJEGREN. THE MOTION PASSED UNANIMOUSLY.

18. Re-Review of Beta Blockers (Green Class)

Dr. Narus said the beta blocker category should be deferred to the next meeting. Sotalol (Sotylize) is a new product and should have been reviewed earlier in the meeting as a red class.

Mr. McCall reported that in November 2015, there were 1,750 claims with 89 percent being preferred agents.

THIS ITEM WAS DEFERRED TO THE NEXT MEETING.

19. Re-Review of Calcium Channel Blockers (Green Class)

Mr. McCall gave the Magellan presentation on Calcium Channel Blockers. There has been nothing new on the market for calcium channel blockers since the last review. Calcium channel blockers have good evidence of reduced mortality in heart disease. There is documented evidence in controlling hypertension. In November 2015, there were 805 claims with 98 percent being preferred agents. At the last review, a motion for therapeutic alternatives, to include at least one dihydropyridine and one nondihydropyridine passed unanimously.

The committee discussed the calcium channel blockers. Dr. Love questioned if an extended release preparation should be included in the motion. Dr. Liljegren agreed it was important to include an extended release preparation, as well as one in the nondihydropyridine and the drugs in the class are not interchangeable.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, TO INCLUDE AT LEAST ONE SHORT-ACTING, ONE EXTENDED RELEASE, AND ONE NONDIHYDROPYRIDINE. SECONDED BY DR. WHITE. THE MOTION PASSED UNANIMOUSLY.

20. Re-Review of Growth Hormone (Green Class)

Mr. McCall gave the Magellan presentation on Growth Hormones. The currently available growth hormone replacement products are, by definition, similar in their clinical effects. There really are no differences. In November 2015, there were 27 claims with 89 percent being preferred agents. At the last review, a motion of class effect passed unanimously.

DR. RUGGLES MOVED A CLASS EFFECT. SECONDED BY DR. LOVE. THE MOTION PASSED UNANIMOUSLY.

21. Re-Review of Bladder Relaxant Preparations (Green Class)

Mr. McCall gave the Magellan presentation on Bladder Relaxant Preparations. There are two different types of bladder relaxants, anticholinergic and a $beta_3$ agonist. Oxybutynin is available as a patch. There is little to no difference in efficacy between the agents. The $beta_3$ agonist has a side effect of hypertension. In November 2015, the claims were 52 percent for preferred agents. About 25 percent of the prescriptions were for Tolterodine (Detrol). At the last review, a motion for therapeutic alternatives passed unanimously.

Dr. Ruggles noted that the majority of the non-preferred usage was for formulations of Detrol. Dr. Narus said the last time the PDL was updated, the price of the generic and the brand might have been very close. We anticipate seeing a shift in the next utilization report.

DR. LOVE MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. RILEY. THE MOTION PASSED UNANIMOUSLY.

The committee thanked everyone for his or her attendance and moved into a closed session.

22. Review Minutes from November 2015 Meetings

There were no changes to the November 2015 meeting minutes.

DR. LOVE MOVED TO APPROVE THE NOVEMBER 2015 MEETING MINUTES. SECONDED BY DR. RUGGLES. WITHOUT OBJECTION, THE MEETING MINUTES WERE APPROVED.

23. Adjourn

WITHOUT OBJECTION, THE MEETING WAS ADJOURNED.

The meeting adjourned at 12:07 p.m.