ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

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

MINUTES OF MEETING
November 20, 2015
8:00 a.m.

Committee Members Present:
Jeffrey Demain, MD, Chair
Jenny Love, MD, Vice Chair
Marvin Bergeson, MD (telephonic)
Robert Carlson, MD (telephonic)
Vincent Greear, R.Ph. (telephonic)
Diane Liljegren, MD (telephonic)
John Pappenheim, MD (telephonic)
Claudia Phillips, MD
John Riley, PA-C (telephonic)
Trish White, R.Ph (telephonic)
Charles Semling, R.Ph.
Jay Butler, MD (non-voting member)

Committee Members Absent:
Robin Cooke, Pharm.D.
Jill Reid, R.Ph
Margaret Rader, CNM

Others Present:
Tina Hawkins, Magellan Medicaid Administration (telephonic)
Erin Narus, State of Alaska
Ryan Ruggles
Vicky Hahn, Kron Associates

1. Call to Order – Chair

Chair Demain called the meeting to order at 8:07 a.m.

2. Roll Call

A quorum was present. Ms. Narus reviewed the rules of the meeting. Chair Demain welcomed everyone to the meeting.

3. Public Comments - Local Public/Health Practitioners

There were no public comments.

4. Re-Review of Pulmonary Arterial Hypertension - Oral and Inhaled (Red Category)

DR. STUART O'BROCHTA, a representative of Gilead Sciences, discussed Letairis (Ambrisentan). The AMBITION trial, which was submitted to the committee, was reviewed. The trial used Ambrisentan with Tadalafil for initial therapy, versus add-on therapy, for pulmonary arterial hypertension (PAH). This is the first time this type of trial has shown positive benefits. The benefit to patients initially starting with Ambrisentan and Tadalafil was a 50 percent reduction in the primary clinical endpoint. The trial and its outcomes were reviewed. The AMBITION trial showed the potential that there has not a class effect between the agents in this class and the ability to use these two specific agents together may be beneficial.

Ms. Hawkins gave the Magellan presentation on Pulmonary Arterial Hypertension - Oral and Inhaled. The treatment for PAH is challenging and complicated, although the number of approved therapies for PAH has grown in the last few years. All agents in this category represent reasonable treatment options. The use of agents in this class may vary depending on the stage of PAH. Another indication for these products is CTEPH, or chronic thromboembolic pulmonary hypertension. Surgery is the only potential cure for CTEPH, but medical therapy has been considered in cases deemed non-operable. In September 2015, there were 7 claims in this class. Significant changes include Tadalafil was contraindicated with guanylate titrate stimulators due to the potential of hypotensive effects in April. In October, Letairis in combination with Adcirca was indicated for the treatment of CAH where it had previously only been indicated for monotherapy. At the last review, a motion for therapeutic alternatives to include one PDE5 inhibitor, one oral non-PDE5 inhibitor, and one inhaled product passed unanimously.

DR. SEMLING MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE ONE PDE5 INHIBITOR, ONE ORAL NON-PDE5 INHIBITOR, AND ONE INHALED PRODUCT. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

5. Re-Review of Antifungals - Oral (Red Category)

There were no public testimonies.

Ms. Hawkins gave the Magellan presentation on Antifungals - Oral. Agents in this class have different spectrums of activity and are FDA approved to treat a variety of infections. Oral antifungals are used in the outpatient setting generally to treat fungal infections such as oropharyngeal candidiasis, urinary tract infections, superficial skin infections, and onychomycosis. In comparative trials, Terbinafine (Lamisil) demonstrated higher treatment success rates for toenail onychomycosis compared to Itraconazole (Sporanox). Terbinafine also demonstrated higher clinical success rates in the treatment of tinea capitis when compared to Griseofulvin; however, Griseofulvin has higher success rates in those infections caused by Microsporum. Isavuconazonium, Posaconazole, Flucytosine, Voriconazole, Itraconazole and Fluconazole are all indicated for more serious fungal infections. Agents in the class have a variety of safety concerns. A black box warning notifying prescribers of potential hepatic toxicities and fatalities in adrenal insufficiency was added to the labeling of oral Posaconazole, resulting in this agent no longer being indicated as first line therapy for any fungal infections. In September 2015, there were 456 claims in this class. Significant changes include Cresemba

(Isavuconazonium Sulfate) was approved in March 2015. It is indicated for the treatment of invasive aspergillosis and invasive mucormycosis. There is no comparative clinical data currently available. In April, Itraconazole's black box warning was expanded to include a warning against the administration to patients with congestive heart failure. At the last review, a motion for therapeutic alternatives passed unanimously.

The committee discussed the class. Dr. Liljegren felt the motion should include oral Terbinafine and Fluconazole based on the new information presented. Terbinafine does not have black box warnings, and it is effective and inexpensive. Although Terbinafine is currently on the preferred drug list, she wanted to ensure it was not removed.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, TO INCLUDE ONE FLUCONAZOLE AND ONE ORAL TERBINAFINE PREPARATION. SECONDED BY DR. GREEAR.

DR. LILJEGREN AMENDED THE MOTION TO MOVE THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, TO INCLUDE AT LEAST ONE FLUCONAZOLE TABLET PREPARATION, ONE ORAL TERBINAFINE PREPARATION, AND ONE PEDIATRIC PREPARATION. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

6. Re-Review of Antidepressant, Other (Red Category)

There were no public testimonies.

Ms. Hawkins gave the Magellan presentation on Antidepressant, Other. The agents in this class inhibit reuptake or block neurotransmitters such as dopamine, serotonin and norepinephrine. All agents in this class, with the exception of Clomipramine, are indicated for the treatment of depression. Clomipramine is only indicated for obsessive-compulsive disorder. While effectiveness is generally comparable within the class, the agents differ in adverse event profiles and safety profiles so the characteristics should be considered when choosing initial therapy. Other factors to consider include primary action profiles, pharmacokinetics, patient preferences and historical patient response. Adverse events reported with Viibryd appear to be similar to those reported with other SSRIs. Venlafazine is associated with higher rates of nausea, which can disappear after about two weeks of therapy. When compared to other antidepressants, Bupropion appears to have the lowest risk of sexual adverse effects and weight gain. Mirtazapine, Nefazodone and Trazodone appear to have the highest risk of sedation. In September 2015, there were just over 2,300 claims in this class. Significant changes include generic Desvenlafaxine ER became available in March 2014. Khedezla, another Desvenlafaxine ER-based product, became available in both brand and generic in April. At the last review, a motion for therapeutic alternatives passed unanimously.

In response to Dr. Liljegren, Ms. Narus said physicians are still allowed to prescribe non-preferred medications utilizing the medical necessary clause. There are no specific reports of problems when using the medical necessary clause. Dr. Demain noted that 92 percent of the prescriptions in 2015 were for drugs on the PDL, which indicates a good job has been done in providing a variety of drugs for patients.

DR. PAPPENHEIM MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY BERGESON. THE MOTION PASSED UNANIMOUSLY.

7. Re-Review of Antipsychotics (Red Class)

MALAAK BRUBAKER, a representative of Otsuka America Pharmaceuticals, discussed Rexulti (Brexpiprazole). Rexulti is an atypical antipsychotic indicated for the treatment of schizophrenia and as an adjunctive treatment to antidepressants for adults with major depressive disorder. The mechanism of action of Brexpiprazole in the treatment of MDD or schizophrenia is unknown. However, the efficacy of Brexpiprazole may be mediated through a combination of partial agonist activity at serotonin 5-HT1A and dopamine D2 receptors, and antagonist activity at serotonin 5-HT2A receptors. A clinical trial and its outcomes was reviewed in which the efficacy of Rexulti in adjunctive treatment of was evaluated in adult patients meeting DSM-IV-TR criteria for MDD, with or without symptoms of anxiety, who had an inadequate response to prior antidepressant therapy and demonstrated an inadequate response throughout the eight weeks of prospective antidepressant treatment. The most common adverse reaction reported was weight increase. Black box warnings include increased mortality in elderly patients with dementia-related psychosis and suicidal thoughts and behaviors in children, adolescents, and young adults. For complete boxed warnings, the full prescribing information is available. We request that Rexulti be included on the Alaska PDL. In July 2015, Abilify became available in a prefilled, dual-chamber syringe for all-in-one reconstitution and administration in both gluteus and deltoid muscles. Additional medical information can be provided upon request.

In response to Dr. Pappenheim, Ms. Brubaker said weight gain for the MDD indication averaged 2.9 pounds at 26 weeks and 3.1 pounds at 52 weeks, with 30 percent gaining at least 7 percent of their body weight and 4 percent losing weight. For the indication for schizophrenia, the weight gain was 1.9 pounds at 26 weeks and 2.1 pounds at 52 weeks, with 20 percent gaining at least 7 percent of their body weight and 10 percent losing 7 percent of their body weight. Ms. Brubaker then went on to discuss the difference between dopaminergic antagonist activity and agonist activity.

(Those attending the meeting telephonically disconnect and called back into the meeting due to background music interrupting the meeting. All members were reconnected except Dr. Riley.)

KAREN NISHAHARA, a representative of Alkermes, discussed Aristada, a long-acting injectable suspension of Aripiprazole. Aristada is indicated for the treatment of schizophrenia and is a pro drug of Aripiprazole. The mechanism of action of Aristada was discussed. The efficacy of Aristada is based on a 12-week trial published in 2015 in the Journal of Clinical Psychiatry. The trial and its outcomes were reviewed. The most common adverse events were insomnia, akathisia and headache. Akathisia, the mostly commonly observed adverse event, occurred in more than 5 percent of the patients. Injection site reactions were reported by 4 to 5 percent of patients, depending on the dosage, compared to 2 percent of patients treated with placebo. Most injection site reactions were injection site pain. Elderly patients treated with antipsychotic drugs are at an increased risk of death. Aristada has a boxed warning for increased mortality in elderly patients with dementia-related psychosis and is not approved for those patients. Tolerability should be established with oral Aripiprazole prior to initiating treatment with Aristada, which may take up to two weeks to fully assess. Treatment dosages, which can be administered monthly or every six weeks, were reviewed. According to ADA guidelines, patients with recurrent relapses related to noncompliance are candidates for long-acting injectable antipsychotics. The Texas Medication Algorithm Project recommends long-acting injectable antipsychotics for

patients who are inadequately adherent at any stage of schizophrenia. Aristada is available in a prefilled syringe and does not require refrigeration. It is contraindicated in patients who have a known hypersensitivity to Aripiprazole. We request your consideration to minimize restriction relative to Aristada.

In response to Dr. Demain, Ms. Nishihara said Aristada should be administered by health care professionals on an outpatient basis.

In response to Dr. Love, Ms. Nishihara described how Aristada was developed. It comes in three strengths in prefilled syringes that do not require reconstitution. It has a three-year shelf life. It can be given either once a month or once every six weeks.

DR. DAVID BLOOM, a representative of AstraZeneca, discussed Seroquel XR extended release tablets. Seroquel XR is indicated for treatment of bipolar disorder and major depressive disorder. It is indicated as monotherapy for the acute treatment of depressive episodes in adults with bipolar disorder. The recommended dose for bipolar depression is 300 milligrams a day. It is also FDA approved in adults for the treatment of acute manic or mixed bipolar I disorder as monotherapy or adjunctive therapy to Lithium or Divalproex. It is also FDA approved for the treatment of acute manic episodes in bipolar I disorder in children and adolescents, ages 10 to 17, as monotherapy. It is FDA approved for the maintenance treatment of bipolar I disorder as adjunctive therapy to Lithium or Divalproex. It is also FDA approved for the treatment of schizophrenia as monotherapy in adults, as well as adolescents ages 13 to 17. Seroquel and Seroquel XR have different dosing and approved indications, which are not interchangeable. Seroquel XR is also indicated as adjunctive treatment to antidepressant therapy in adults with major depressive disorder and offers a treatment option for patients with inadequate response to antidepressant therapy. The recommended dose for adjunctive major depressive disorder is 150 to 300 milligrams per day. The most common adverse reactions in adults were somnolence, dry mouth, constipation, dizziness, increased appetite and weight gain. The most common adverse reactions in children were somnolence, dizziness, fatigue, increased appetite, nausea, vomiting, dry mouth, and weight increase. The committee should refer to the prescribing information for further product information and boxed warnings. It is AstraZeneca's position that patients stabilized on a particular drug regimen should continue to receive the therapy that works for them. Due to the vulnerability of the mental health disorder population, it is important that stabilized care continues. We request consideration of maintaining Seroquel XR on the Alaska PDL.

ALLEN WU, a representative of Janssen Medical Affairs, discussed Invega Trinza, a three-month injection indicated for the treatment of schizophrenia that was approved in May 2015. It comes in prefilled syringes. It can be administered in the deltoid or gluteus muscles. It has four dosages. The medium apparent half-life of Invega Trinza was reviewed. It may be administered up to seven days before the time of the next scheduled injection or one month flexible dosing during the maintenance phase. Invega Trinza was approved based on a phase-three clinic trial published in General Psychiatry in March 2015. The trial and its outcomes were reviewed. Adverse reactions included injection site reactions, weight gain, akathisia and headaches.

DR. KIM LAUVMEIER, a representative of Sunovion Pharmaceutical, discussed Latuda (Lurasidone). Latuda is indicated for the acute treatment of schizophrenia and bipolar depression in adults and is the only agent in this class with an indication as both monotherapy and adjunctive therapy with Lithium or Divalproex for the acute treatment of bipolar depression. It is the only atypical

antipsychotic, other than Clozapine, with a pregnancy category D rating. Latuda has no clinically relevant impact on QTP interval and smoking is not expected to have an effect on its pharmacokinetics. The safety and efficacy of Latuda has been established in numerous clinical trials. The committee should refer to the full prescribing information for a complete list of warnings, precautions, and adverse events. Latuda has consistently demonstrated cost effectiveness and positive outcomes for adult patients with schizophrenia and bipolar depression. Several trials and their outcomes were reviewed. An independent article published in the Academy of Managed Care Pharmacy Peer Reviewed Journal in September 2015 concluded that Latuda was observed to have medical cost savings when compared with other second-generation antipsychotics; and when initiating patients on a second-generation antipsychotic, Latuda should be considered. Latuda addresses the need for safe and cost-effective agents to manage patients. We respectfully ask that you allow Medicaid's patients unrestricted access to Latuda.

Ms. Hawkins gave the Magellan presentation on Antipsychotics. Agents within the antipsychotic class have varying indications. They are approved for schizophrenia, bipolar disorder, other psychotic disorders, as well as depression and irritability associated with autistic disorder. The first generation of agents can be classified according to their affinities for the dopamine type 2 receptors. The second-generation antipsychotics have more selectivity in targeting the intended mesolimbic D_2 pathway compared to the first. They also block or partially block 5-HT_{2A} and 5-HT_{1A} serotonin receptors with greater affinity for the 5-HT_2 receptors. Second generation antipsychotics have reduce incidents of extrapyramidal side effects and less impact on prolactin levels. Ingestible forms of these products are generally used to increase compliance and vary in regards to route administration and dosing schedules. In September 2015, there were 3,066 claims in this class, with 99.1 percent being preferred agents. Significant changes since the last review include the FDA approval of Invega Trinza, which is indicated for the treatment of schizophrenia. It is administered intramuscularly every three months by health care professionals. Another new product is Rexulti, which is indicated for the treatment of schizophrenia and as adjunct therapy to antidepressants for the treatment of major depressive disorder. At the last review, a motion for therapeutic alternatives to include one oral solution product and one long-acting injectable product, not Zyprexa Relprevv, and the motion passed unanimously.

Dr. Pappenheim clarified the highlighted statement near the bottom of page 10 of the TCR materials. "Brexpiprazole (Rexulti) is pharmacologically similar to Aripiprazole (Abilify, Ability Maintena); both are partial dopamine and 5-HT_{1A} agonists rather than full dopamine ~~agonists~~ antagonists.

Dr. Phillips noted that Saphris had an indication for childhood bipolar disorder, which was not notated in the TCR materials. (indiscernable) and Aristada do not seem to pull away from the other drugs and may not be good drugs to prefer, but they would probably be prescribed by the adult providers instead of pediatric providers. Trinza deserves consideration because it has the potential to increase compliance for patients with schizophrenia who are notoriously difficult to treat.

Dr. Carlson expressed concerned about short studies on possible lifetime illnesses. They are good starting points, but the data on efficacy and side effects are inadequate to make real clinical decisions.

In response to Dr. Demain, Dr. Carlson said there needs to be long-term side-by-side studies when it comes to long-term efficacy and side effects to make real clinical decisions that might affect a person for many years.

Dr. Pappenheim said the same problem existed across the spectrum of medicine. We do not know what the effect of a drug will be in 20 years. We only know what its effect has been in the six to eight weeks when it receives FDA approval. Drugs not on the PDL can still be prescribed utilizing the medically necessary clause.

Dr. Carlson said these drugs have different side effects; and different individuals will have different responses to the same drug.

DR. PAPPENHEIM MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE ORAL AGENT, AT LEAST ONE ORAL SOLUTION, AT LEAST ONE SHORT-ACTING INJECTABLE, AND AT LEAST ONE LONG-ACTING INJECTABLE FORMULATION. SECONDED BY DR. LOVE. THE MOTION PASSED UNANIMOUSLY.

8. Re-Review of Hypoglycemics - Incretin Mimetics/Enhancers (Red Class)

Ms. Narus read a letter from Dr. J. Ross Tanner, of the Diabetes and Lipid Clinic of Alaska, advocating for an alternative once-weekly GLP agonists on the Alaska PDL.

Ms. Narus read an email from Dr. Ilona Farr, a family practice physician, advocating that all the once-weekly GLP-1 medications be added to the Alaska PDL.

DANIELLE DAY, a representative of AstraZeneca, discussed Bydureon, which is the continuous release formation of Exenatide and is the same active ingredient in Byetta. As a GLP-1 receptor agonist, Bydureon stimulates glucose-dependent insulin secretion from the pancreatic beta cells, suppresses inappropriately elevated glucagon levels, and slows gastric emptying. Bydureon was approved in January 2012 by the FDA. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. It is administered as a subcutaneous injection, 2 milligrams once every seven days, at any time of day, without regard to meals. It comes in two forms. The single dose tray includes a prefilled syringe and vial. The Bydureon pen, which was approved in February 2014, is a single-use injector that eliminates the need for patients to transfer the medication between a vial and a syringe. Several studies and their outcomes were reviewed. The key adverse events with Bydureon are nausea, diarrhea and injection site reactions. The six-year data also shows that these events decrease over time. Bydureon has a boxed warning for thyroid C-cell tumors and post-marketing reports of acute pancreatitis. It is advised that patients be monitored for pancreatitis and Bydureon be discontinued if signs or symptoms exist. Other information on safety can be found in the package insert.

In response to Dr. Demain, Ms. Day said Bydureon was dosed once a week instead of daily. There is also significantly lower nausea rates and weight loss with Bydureon versus Byetta.

CRAIG SEXTON, a representative of GlaxoSmithKline, discussed Tanzeum (Albiglutide). Tanzeum is a GLP-1 receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. Please see the package insert for the full limitations of use, important safety information including the black box warning for the risk of thyroid C-cell tumors, contraindications and adverse reactions. Several trials and their outcomes were reviewed. We believe that Tanzeum provides a unique and important option for patients and clinicians facing the important

decision point of progressing to mealtime insulin and would ask that the committee recommend once-weekly Tanzeum for inclusion on the Alaska PDL.

JOHNNY SAWADA, a representative of Boehringer Ingelheim, discussed Linagliptin, a DPP-4 inhibitor indicated as an adjunctive treatment to diet and exercise to improve glycemic control in adults with type 2 diabetes. Several studies and their outcomes were reviewed. Linagliptin has a demonstrated safety profile. The adverse reactions reported included nasal pharyngitis, diarrhea, and a cough. A unique feature of Linagliptin is it is a single strength DPP-4 inhibitor with a daily 5-milligram dose, taken with or without food, as both the starting dose and maintenance dose, and it comes without any required dosage estimates in patients with declining renal function or hepatic impairment. We request that Linagliptin be added to the Alaska PDL.

Ms. Hawkins gave the Magellan presentation on Hypoglycemics - Incretin Mimetics/Enhancers. There are three subclasses in this category: GLP-1 receptor agonists, the DPP-4 enzyme inhibitors and Amylin analogues. The GLP-1 receptor agonists are indicated for patients with type 2 diabetes. Administration of Albiglutide is associated with HbA1c reduction of 0.7 to 0.9 percent, Dulaglutide with a reduction of 0.7 to 1.6 percent, and Exenatide and Liraglutide with a reduction of 0.5 to 1.6 percent based on clinical trials. Many study participants experience a decrease in weight gain of about 0.4 to 3.5 kilograms from baseline. Hypoglycemia is not usually associated with GLP-1 agonist therapy unless they are using combinations. GLP-1 agonists are administered by subcutaneous injection. Byetta is dosed twice daily. Victoza is dosed once daily. Tanzeum, Trulicity and Bydureon are dosed once weekly. The DPP-4 inhibitors are indicated for adult patients with type 2 diabetes. DPP-4 inhibitors have modest glucose lowering effects with hemoglobin A1C reductions of 0.5 to 1.0 percent. These agents are weight-neutral and have a lower hypoglycemia risk when used as monotherapy or in conjunction with Metformin. Symlin is the only A1 analog and it is approved for the management of type 2 diabetes as well as type 1 diabetes. It is indicated to be co-administered with mealtime insulin and in the setting where there is an increased risk of severe hypoglycemia. Hemoglobin A1C improvements are about 0.3 to 0.6 percent with potential weight reductions of about 0.5 to 1.5 kilograms. This product should not be used in patients with confirmed gastroparesis. In September 2015, there were 220 claims. Significant changes include the availability of Trulicity in October 2014. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. There are no comparative clinical trials available in published journals. There is an extensive manufacturer approval study on Trulicity, which was reviewed. Glyxambi is also a new product in this class. It is the combination of Linagliptin and Empagliflozin. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes when appropriate. It is given once daily in the morning. There are no comparative studies available yet. In September, the FDA issued a warning for DPP-4 inhibitors regarding severe and disabling joint pain. Prescribing information for these products has been updated. At the last review, a motion for therapeutic alternatives to include one GLP-1 and one DPP-4 passed unanimously.

Dr. Love wondered if the subclasses in this category was going to become too large to review and would need to be separated in the future.

Dr. Liljegren referenced the letter from Dr. J. Ross Tanner and questioned if patients were able to get the GLP-1 injections when their doctor deemed it medically necessary. Dr. Semling said the injections were non-preferred but could be prescribed utilizing the medically necessary clause. Ms. Narus said

there were no prior authorization requirements for GLP-1 injections and physicians could utilize the medically necessary clause.

DR. SEMLING MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE ONE GLP-1 AND ONE DPP-4. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

9. Re-review of Hypoglycemics - Insulin and Related Agents (Red Class)

ANTHONY HOOVLER, a representative of Novo Nordisk, discussed Tresiba, a new long-acting basal insulin analog approved in September 2015. It is indicated to improve glycemic control in adult patients with diabetes. It is not currently approved for use in children or adolescents. It is pregnancy category C. As with other insulins, hypoglycemia is the most common adverse reaction with Tresiba. Please see the PI for additional safety information. Several trials and their outcomes were reviewed. Many properties of Tresiba make it unique among the basal insulin class. It has a mean half-life of approximately 25 hours and a duration of action of at least 42 hours; both values are the longest among the basal insulin class. Tresiba is administered once daily. However, unlike other once-daily basal insulin analogs that must be administered at the same time of day by label, Tresiba may be administered at any time of day. It is available two formulations, both in a flex-touch pen device. The option to provide 160 units in a single injection is unique to Tresiba. As the two formulations were engineered to be bioequivalent, there is no requirement to perform a dose conversion when using either the Tresiba U-100 or U-200 pens. The pen dose window shows the number of insulin units to be delivered. Recommended starting doses were reviewed. After being open, the flex-touch pen may be used up to 56 days, which is 14 days longer than any other commercially available basal insulin analog. We respectfully request consideration that you make Tresiba a preferred drug on the Alaska PDL.

In response to Ms. Narus, Ms. Hawkins said a new drug update on Tresiba could be available by the January 2016 meeting.

Dr. Demain noted that Tresiba had not made the list of drugs to be reviewed due to the date the FDA approved it in relation to the meeting date. It was decided the classification would be tabled to the January 2016 meeting so Tresiba can be included in the review.

10. Re-review of Hypoglycemics - SGLT2 Inhibitors (Red Class)

DANIELLE DAY, a representative of AstraZeneca, discussed Farxiga (Dapagliflozin). Farxiga is a sodium-glucose cotransporter 2 inhibitor (SGLT2) that works in the kidney to block re-absorption of glucose back into the blood and send it out through the urine, thus lowing the glucose concentrations. Farxiga was FDA approved in January 2014. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. The recommended starting dose is a 5-milligram oral tablet taken every morning, regardless of food. Patients tolerating the 5-milligram dose who are looking for more glycemic control can be increased to a 10-milligram dose. Several trials and their outcomes were reviewed. Farxiga is not indicated for weight loss or hypertension. The most common adverse events were female genital mycotic infections, nasopharyngitis, and urinary tract infections. The package insert can be referred to for further safety information.

Ms. Narus read a letter from Dr. Robert Skala, of True North Medicine, advocating for the inclusion of Jardiance (Empagliflozin) on the Alaska PDL.

JOHNNY SAWADA, a representative of Boehringer Ingelheim, discussed Jardiance (Empagliflozin). Empagliflozin is an SGLT2 inhibitor indicated for the improvement of glycemic control in adults with type 2 diabetes. Several studies and their outcomes were reviewed. Dosages are 10 and 25 milligrams, once daily, with or without food. The package insert submitted to the committee is dated June 2015 and is the most recent one available. Under the warnings and precautions section, an update will be made based on a study done in September 2015 regarding the lack of clinical studies establishing conclusive evidence of macrovascular risk reduction in Jardiance or any other anti-diabetic drug.

Ms. Hawkins gave the Magellan presentation on Hypoglycemics - SGLT2 Inhibitors. Sodium-glucose cotransporter 2 inhibitors are indicated as an adjunctive to diet and exercise to improve glycemic control in adults with type 2 diabetes. According to the American Diabetes Association, if monotherapy with Metformin at a maximum tolerated dose does not achieve or maintain the desired A1C levels over three months, either a TZD, a sulfonylurea, a DPP-4 inhibitor, an SGLT2 inhibitor, DLP-1 or insulin should be added. If A1C is still not achieved after an additional three months then an agent from a different group should be added. Significant changes in the class include the addition of Xigduo to the marketplace. In May 2015, the FDA cautioned that the GLP-2 inhibitors might cause ketoacidosis, which they continue to investigate. Synjardy, which is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes who are not adequately controlled on a regimen containing Jardiance or Metformin or in patients already taking both of those products, was approved in September. Synjardy is dosed twice daily with meals. Invokana labeling now includes a warning regarding the increased risk of bone fractures and decreased bone mineral density. The FDA will continue to monitor all the SGLT2s for this risk. The INFERRED OUTCOME, which was a manufacturer-funded studied published in the New England Journal of Medicine, compared Jardiance to placebo with standard of care in type 2 diabetics at high risk for cardiovascular events, was reviewed. At the last review, a motion for therapeutic equivalence passed unanimously.

DR. RILEY MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC EQUIVALENCE. SECONDED BY DR. LOVE.

In response to Dr. Love, Ms. Narus said there were no utilization statistics provided because there did not appear to be any utilization of these drugs in the comparator timeframe.

THE MOTION PASSED UNANIMOUSLY WITH ONE ABSTAINING.

Break from 9:53 a.m. to 10:09 a.m.

11. Re-Review Neuropathic Pain (Red Class)

There were no public testimonies.

Ms. Hawkins gave the Magellan presentation on Neuropathic Pain. Neuropathic pain can be caused by a number of different diseases such as post-herpetic neuralgia, diabetes and fibromyalgia. There is limited comparative head-to-head data on neuropathic pain. Various professional guidelines suggest different first line and second line treatments based on indication. These include tricyclic

antidepressants, Gabapentin, Pregabalin, opioids, Lidocaine 5% transdermal patches, Duloxetine, and topical Capsaicin. When selecting a drug, consideration should be given to other factors such as adverse event profiles, ability to treat comorbid conditions, drug-to-drug interactions, and contraindications. In September 2015, there were about 2,300 claims in this class. Significant changes include Irenka was approved by the FDA. It is indicated for the treatment of major depressive disorder, generalized anxiety disorder, diabetic personal neuropathy, and chronic musculoskeletal pain. Irenka is dosed once or twice daily and comes in a 40-milligram, delayed-released capsule. In June 2015, Irenka became available as a generic. At the last review, a motion for therapeutic alternatives passed unanimously.

In response to Dr. Demain, Ms. Narus discussed how medications on the PDL were categorized. While some medications can be used for other indications, the medications are categorized based on a rebating perspective.

In response to Dr. Pappenheim, Ms. Narus discussed page 14 of the TCR where Duloxetine's dosage is listed as 60 milligrams once daily but Dr. Pappenheim noted that it was not uncommon to prescribe up to 120 milligrams a day. Setting dosage limitations is under the purview of the Drug Utilization Review Committee and the prescriptions should be filled until they set a limitation.

In response to Dr. Riley's question regarding Irenka being provided in a 40-milligram capsule, but dosed at 60 milligrams a day, Ms. Hawkins said she would check to see if the information was correct.

Dr. Demain asked for comments related to all of the neuropathic pain therapies on the approved PDL being oral formulations and no topical formulations. Ms. Narus said Lidocaine, the topical agent in the non-preferred section, has an FDA indication for post-herpetic neuralgia and the product has a prior authorization requirement.

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

12. Re-Review of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) (Red Class)

There were no public testimonies.

Ms. Hawkins gave the Magellan presentation on Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Nonsteroidal anti-inflammatory drugs are commonly used to treat rheumatoid arthritis, osteoarthritis, and pain from various etiologies. While agents in the class have varying FDA-approved indications and safety profiles, the available clinical data does not suggest that any one NSAID offers a clear advantage in terms of safety or efficacy. There are complex tradeoffs between the benefits, such as pain relief, improved function, and improved tolerability, and potential harms, such as cardiovascular, renal and gastrointestinal issues. If the risk of gastrointestinal adverse events is increased, the topical route is preferred. When weighing the potential effects of any of these agents, the following patient factors should be considered prior to initiation of therapy: age, comorbid conditions, and concomitant medications. In September 2015, there were almost 2,400 claims in this class. Significant changes include the FDA approval of Tivorbex in May 2015. Tivorbex is an Indomethacin product that is indicated for the treatment of mild to moderate acute pain in adults. It is given two to three times daily.

DermacinRx Lexitral was introduced in July 2015 and is a kit that contains Diclofenac drops and a Capsaicin cream. At the last review, a motion for therapeutic alternatives to include a topical and Celecoxib passed unanimously.

Dr. Demain said Celecoxib was not on the current PDL, but there was a COX-2 inhibitor. He questioned if the committee really just wanted a COX-2 inhibitor on the PDL.

DR. RILEY MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE ONE TOPICAL FORMULATION AND ONE COX-2 INHIBITOR. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

13. Re-Review of Analgesics - Narcotics Long-Acting (Red Class)

DR. ROY PALMER, a representative of Pfizer, discussed Embeda. The long-acting opioid class is different as there is no available evidence that there are differences in efficacy or safety between these agents when dosed at equal doses. The big issue is the risk of abuse, misuse and diversion. Alaska, like the other states, has a problem with prescription drug abuse and heroin abuse. Data from the NSTUH indicates that 75 to 80 percent of heroin abuse is started by abusing prescription opioids. In an attempt to mitigate this problem, the pharmaceutical industry is trying to make these drugs less appealing and less prone to abuse. The FDA and the CDC have prioritized the development of safer and less abuse prone opioids as a priority. The FDA has issues guidance as to how to test these drugs. Labeling for package inserts is based on various levels of evidence and clinical studies. Embeda has a category 3 labeling, which is the highest level anyone has attained to date. Embeda is an extended-release Morphine product that contains pellets of Morphine sulfate with a sequestered core of Naltrexone. If taken orally and without manipulation, the drug is not absorbed and passes through the GI, providing the Morphine effect with no impact of the Naltrexone. If the pill is crushed in an attempt to snort or inject it, the Naltrexone is released and acts as an antagonist to the opioid receptors, reducing euphoria. Several studies and their outcomes were reviewed. Given these drugs are therapeutically equivalent, one or more abuse-deterrent opioids should be available on the Alaska PDL.

In response to Dr. Demain's amazement that a study was approved that gave drug-addicted people Morphine to see which ones they preferred, Dr. Palmer clarified that the participants in the study were not addicted to drugs, but were recreational users.

Ms. Hawkins gave the Magellan presentation on Analgesics - Narcotics Long-Acting. Long-acting narcotics are indicated for use in the management of pain severe enough to require daily, around-the-clock treatment, and for which alternative therapies are inadequate. The World Health Organization's guideline for cancer pain management recommends a three-stepped approach with consideration for the type of pain and response to therapy. Initial therapy should include non-opioid analgesics, such as non-steroidal anti-inflammatory drugs (NSAIDs). For mild to moderate pain, oral combinations of Acetaminophen and NSAIDs with opioids are recommended. For moderate to severe pain, opioid analgesics are the treatment of choice. Despite attempts to produce a product that reduces abuse, no data exists that distinguishes any of these products from others. The following medications are available as abuse-deterrent formulations: Embeda capsules; Hysingla ER tablets; OxyContin biconcave tablets; Oxycodone ER tablets, and Zohydro ER abuse-deterrent capsules. In September 2015, there were 718 claims in this class. Significant changes include the approval of Hysingla ER in December 2014. Hysingla ER is indicated for the management of severe pain that requires around-the-

clock, long-term opioid treatment. It is dosed once daily, starting at 20 milligrams. In August 2015, OxyContin gained FDA approval for patients 11 years of age and older, whereas previously it was only indicated for adults. At the last review, a motion for therapeutic alternatives to include one transdermal product passed unanimously.

Ms. Narus read a letter from Dr. Ginger Scroggins, of the Manuka Health Clinic, advocating for the inclusion of Butrans (Buprenorphine transdermal), which she uses for the treatment of chronic disseminated Lyme disease, on the Alaska PDL.

Dr. Demain noted that Butrans was a schedule III narcotic. Ms. Hawkins said there were five medications in the category that were considered abuse deterrents: Embeda, Hysingla ER, OxyContin biconcave tablets, Oxycodone ER tablet, and Zohydro ER.

The committee discussed including abuse-deterrent formulation on the PDL. Dr. Love felt the committee should express a preference for the abuse-deterrent formulations. Dr. Demain said there was a significant rise in heroin use in Alaska so it would be beneficial to have abuse-deterrent drugs available. Dr. Carlson said Washington state had new guidelines for opioid prescribing which should be reviewed. Mr. Butler said there were national guidelines that would be issued from the CDC in January 2016 that will be focused on pain management using opioids. Dr. Pappenheim felt Butrans could easily be replaced by Suboxone, an oral formulation that is almost impossible to abuse and provides the same pain relief as straight Buprenorphine if used appropriately. Dr. Phillips agreed that the committee should express a preference for the abuse-deterrent formulations in this class. The committee further discussed the Washington state and upcoming CDC guidelines. Dr. Butler did not recall there being a focus on abuse deterrent formulations in the Washington guidelines. It was noted that restrictions in this class were the purview of the DUR Committee. Dr. Love discussed how the motion could be written to change the PDL and prefer abuse-deterrent formulations. Ms. Narus said the motion should be clear whether the PDL would only include abuse-deterrent formulations or if they would just be an option.

DR. LOVE MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE TRANSDERMAL PREPARATION AND ONE ABUSE-DETERRENT PREPARATION. SECONDED BY DR. LILJEGREN. THE MOTION PASSED WITH ONE OPPOSED.

14. Re-Review of Opiate Dependence Treatments (Red Class)

DR. NICK CASALI, a representative of Indivior, discussed Suboxone Sublingual Film, which was FDA approved in 2010 for the maintenance treatment of opioid dependence. In April 2014, the FDA updated our indication and Suboxone Sublingual Film is now indicated for the complete treatment of opioid dependence. In September 2015, the FDA approved a labeling revision to Section 2.3 of Suboxone Sublingual Film's package insert which relates to inducing and administration of our product. It can now be delivered sublingually, under the tongue, or buccally. For our new method of buccal administration, patients should be instructed to place one film on the inside of the left or right cheek. If an additional film is necessary, the additional film is to be placed on the inside of the opposite cheek. Abuse and diversion of Buprenorphine containing products has been a concern of P&T committees nationwide. Several studies on abuse, addiction and diversion were reviewed. Please consult our package insert for all safety and prescribing information.

Ms. Hawkins gave the Magellan presentation on Opiate Dependence Treatments. Opiate dependence treatments are indicated for the treatment of opiate dependency. Buprenorphine is a partial agonist, Naloxone is an antagonist, and Naltrexone is an opioid antagonist. Buprenorphine, a schedule III product, is listed under the Controlled Substance Act and has the same potential for abuse as opioids. Both Buprenorphine and Buprenorphine/Naloxone can be used for office-based detoxification from opiates and maintenance treatment for opiate dependency by specially trained and registered physicians. Like Methadone, Buprenorphine can suppress opiate withdrawal symptoms and block the effects of other opiates. Naltrexone is used to help maintain an opiate-free state in patients who are known opiate abusers, but it does not prevent withdrawals. Patients with severe opiate dependency may be considered for alternative therapy. In September 2015, there were 588 claims in this class. Significant changes include the FDA approval of Bunavail in July 2015. Bunavail is a combination product containing Buprenorphine and Naloxone. There is no comparative data for Bunavail. Zubsolv gained an indication for initial treatment as opioid dependency in August 2015. Previously, it had only been indicated for maintenance therapy. Evzio, a Naloxone injection, is delivered by a handheld auto injector containing Naloxone that is indicated for the emergency treatment of opioid overdose, either known or suspected. Evzio is not intended as a substitute for emergency medical care. At the last review, a motion for therapeutic alternatives passed unanimously.

In response to Dr. Demain, Ms. Hawkins said the drugs in this class were not indicated for pain management and should not be used for anything other than opiate dependence. The committee discussed when an IM was used instead of a sublingual formulation.

Ms. Narus explained that Methadone was included in the long-acting narcotic analgesics category due to the bidding process, but was also a covered treatment for opioid dependence.

DR. PAPPENHEIM MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

15. Re-Review of Stimulants and Related Agents (Red Class)

Ms. Hawkins gave the Magellan presentation on Stimulants and Related Agents. The FDA approved indications for the stimulants and related agents vary regarding the age of treatment. All of these products have similar efficacy and adverse events. Current guidelines make no differentiation between available products, formulations or dosage forms. Studies have shown that 70 to 75 percent of patients respond to the first stimulant medication of which they are started. Response rates then increase to about 90 to 95 percent when a second stimulant is tried. Treatment failures with stimulants are often due to improper dosing rather than ineffectiveness of the medication. It may also take one to three months to actually establish the best dose and form of medication for any given patient. The treatment alternatives for narcolepsy were reviewed. According to the current literature, Provigil or Nuvigil may be better tolerated and preferred over traditional stimulants for the treatment of excessive daytime sleeping. In September 2015, there were 2,058 claims in this category, with about 96 percent of those being preferred products. Significant changes include Evekeo was approved in February 2015. It is indicated for the treatment of narcolepsy ADHD. It is dosed once or twice daily in divided doses. It is available in 5 and 10-milligram tablets. There is no comparative clinical data available on Evekeo. Aptensio XR is indicated for the treatment of ADHD in patients 6 years and older. Contraindications,

warnings, adverse effects, and drug interactions are similar to those of other controlled released Methylphenidate products. In June, Daytrana had a new warning added to its label for potential permanent skin color loss that can range up to 8 inches in diameter. At the last review, a motion for therapeutic alternatives to include one extended release stimulant product, one non-stimulant product, in addition to an extended release alpha agonist, passed unanimously.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE ONE EXTENDED RELEASE STIMULANT PRODUCT, ONE NON-STIMULANT PRODUCT, IN ADDITION TO AN EXTENDED RELEASE ALPHA AGONIST. SECONDED BY DR. LOVE. THE MOTION PASSED UNANIMOUSLY.

16. Re-Review of Sedative Hypnotics (Red Class)

Ms. Hawkins gave the Magellan presentation on Sedative Hypnotics. Sedative hypnotics have been shown to be effective in treating insomnia. The agents differ in their side effect profiles, onset and duration of action, as well as clinical outcome data. Selection of a specific product in this category is generally based on whether the patient has problems with initiation or maintenance of sleep, as well as comorbid conditions, side effects, tolerance and availability. In September 2015, there were 737 claims in this class. Significant changes include the approval of Belsomra in December 2014. Belsomra is indicated for the treatment of insomnia characterized by difficulty in sleep onset, with or without sleep maintenance issues. There is no comparative clinical data for Belsomra. At the last review, a motion for therapeutic alternatives passed unanimously.

In response to Dr. Demain, Ms. Narus said the question of whether Ambien dosages had to be reduced for women was addressed by the DUR Committee about two and a half years ago. Letters were sent to the prescribers to alert them of the issue.

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

Break from 10:58 a.m. to 11:05 a.m.

The meeting was called back to order at 11:05 a.m. by Vice Chair Love, as Chair Demain had to leave.

17. Re-Review of Hypoglycemics - TZDs (Green Class)

Ms. Hawkins gave the Magellan presentation on Hypoglycemics - TZDs. All of the TZDs are indicated for the treatment of type 2 diabetes as either mono or combination therapy. At monotherapy, these agents typically produce a reduction in hemoglobin A1C of about 1 to 1.5 percent. They typically reduce fasting plasma glucose levels by about 40 to 60 milligrams per deciliter. In combination with other anti-diabetic agents, the products can be expected to lower hemoglobin A1C by an addition 1 percent and fasting plasma glucose by an addition 25 to 50 milligrams per deciliter. In September 2015, there were 86 claims in this class. Since the last review, there have been no significant changes. At the last review, a motion for therapeutic alternatives passed unanimously.

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

18. Re-Review of Hypoglycemics - Metformin (Green Class)

Ms. Hawkins gave the Magellan presentation on Hypoglycemics - Metformin. Metformin reduces hemoglobin A1C by 1.5 to 2 percent and fasting plasma glucose levels by about 20 percent or 60 to 70 milligrams per deciliter. Metformin also has favorable effects on serum triglycerides, total cholesterol and LDL-C, and a possible modest increase in HDL-C. Metformin is marketed in several delivery systems, which hold slightly different FDA approved indications. However, current treatment guidelines make no differentiation among the products for clinical efficacy or safety. In September 2015, there were a little over 1,200 claims in this category, with the majority of those being Metformin. Since the last review, there were no significant changes. At the last review, a motion for class effect passed unanimously.

DR. BERGESON MOVED A CLASS EFFECT. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

19. Re-Review of Antidepressants, SSRI (Green Class)

Ms. Hawkins gave the Magellan presentation on Antidepressants, SSRI. SSRIs have varying FDA approved indications. However, they are generally considered to have comparable efficacy and are considered first line therapy for their FDA-approved indication. Differences among these products are usually with the side effect profile, half-life, and potential for drug interactions. For example, Paroxetine tends to cause weight gain while Fluoxetine causes weight loss. Paroxetine has the highest rate of sexual adverse events. Fluoxetine is relatively energizing whereas Paroxetine is more sedating and constipating. Fluoxetine has the longest half-life, resulting in the lowest likelihood of discontinuation symptoms if therapy is abruptly stopped. That long half-life also lessens the effect of missed doses. Paroxetine has a shorter half-life, which results in a quicker onset of action, but a higher rate is discontinuation symptoms. Citalopram and Escitalopram tend to have the lowest potential for drug-to-drug interactions and they do not substantially inhibit any of the cytochrome P450 enzyme pathways. Generally, the choice of antidepressant is based on the patient's prior experience with drug treatment and the potential side effects and cost. In September 2015, there were 3,397 claims in this class, with 97 percent being preferred products. At the last review, a motion for therapeutic alternatives to include at least one pediatric indication passed unanimously.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE PEDIATRIC INDICATION. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

20. Re-Review of Anticonvulsants (Green Class)

Ms. Hawkins gave the Magellan presentation on Anticonvulsants. Anticonvulsants have varying FDA approved indications, which include seizure disorders, Lennox-Gastaut Syndrome, migraine prophylaxis, bipolar disorder, and neuropathic pain. Since there is a lack of comparative data for anti-epileptic agents, there really are no standard guidelines from the U.S. to help us differentiate the

superiority of one agent over another for seizure control. The selection of anti-epileptic treatment generally depends on the particular seizure type. In September 2015, there were 3,997 claims in this class, with over 90 percent of them being preferred agents. At the last review, a motion for therapeutic alternatives passed unanimously.

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

21. Review Minutes from April and September 2015 Meetings

Acting Chair Love noted a change to be made to the April 2015 meeting minutes where Budesonide should be listed as a pregnancy category B drug and not a pregnancy category D drug. The committee members had no other changes to the April and September 2015 meeting minutes.

DR. PHILLIPS MOVED TO APPROVE THE APRIL AND SEPTEMBER 2015 MEETING MINUTES. SECONDED BY DR. BERGESON. WITHOUT OBJECTION, THE MEETING MINUTES WERE APPROVED.

22. Comments from Committee Members or Chair

There were no comments from the committee members.

23. Adjourn

DR. PAPPENHEIM MOVED TO ADJOURN THE MEETNG. SECONDED BY DR. BERGESON. WITHOUT OBJECTION, THE MEETING WAS ADJOURNED.

The meeting adjourned at 11:18 a.m.