

**ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE**

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

**MINUTES OF MEETING
November 21, 2014
8:00 a.m.**

Committee Members Present:

Jeffrey Demain, MD - Chair
Robin Cooke, Pharm. D.
Marvin Bergeson, MD
Robert Carlson, MD (telephonic)
Vincent Greear, R.Ph.
Jenny Love, MD (telephonic)
Claudia Phillips, MD
John Riley, PA-C
Chuck Semling, Pharm.D.
Jill Reid, R.Ph (telephonic)
Trish White, R.Ph. (telephonic)
Maggie Rader, CNM
John Pappenheim, MD (telephonic)

Committee Members Absent:

Diane Liljegren, MD

Others Present:

Chad Hope, Pharm.D.
Julie Pritchard, Magellan Medicaid Administration
Tolu Balogun, Magellan Medicaid Administration
Erin Narus, State of Alaska
Adrienne Dahlgren
Pamela Vincent, M.D.
Bob Senecker
David Chatman
Kim Lovemeir
Karen Wyn
John Hofcott

1. Call to Order – Chair

Dr. Dermain called the meeting to order at 8:01 a.m.

2. Roll Call

A quorum was present. Dr. Demain reviewed the rules of the meeting.

3. Public Comments – Local Public/Health Practitioners

Adrienne Dahlgren, on behalf of Andrzej Maciejewski, M.D., commented in support of Invokana, which is used to treat diabetes. She stated it allows a decrease in insulin and weight reduction, and there have been patients who have become more compliant as they have success with weight reduction. Some have come off of blood pressure medication. It is a glucose lowering agent with minimal side effects and does weight reduction.

4. Re-Review of Long-Acting Narcotic Analgesics (Red Class)

There were no public testimonies.

Dr. Balogun gave the Magellan presentation on long-acting narcotic analgesics. All products within this class are indicated for the management of pain severe enough to require daily around-the-clock treatment, and for which alternative treatments are inadequate. When properly used, these agents can decrease administration frequency and the incidents of adverse affects. They can also increase periods of consistent pain control. They have a high potential for abuse and a risk of fatal overdose due to respiratory repression, which usually occurs within the first 24-72 hours after initiation or increase in dose. Long use of opiate analgesics during pregnancy may cause neonatal opioid withdrawal syndrome.

The utilization within this class was 762 claims in September 2014. Significant changes since the last review was that Zohydro ER was approved by FDA October 2013, and has the same indication as the other agents in this class, and categorized as Pregnancy Category C. Consumption of alcohol while taking Zohydro can result in fatal plasma hydrocodone levels. It is contraindicated in patients who have severe respiratory depression. The safety and effectiveness in pediatric patients under the age of 18 has not been established. It is available as a capsule in multiple dosage forms from 10 to 50 mg.

The other significant change in this class is Embeda. It was previously voluntarily withdrawn from the market March 2011, due to testing that found stability concerns in the manufacturing process. In November 2013, the FDA confirmed that these issues were resolved and it was reintroduced into the market.

At the last review, a motion for therapeutic alternatives to include at least one transdermal preparation passed unanimously.

DR. BERGESON MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE ONE TRANSDERMAL PRODUCT. SECONDED BY DR. PHILIPS. THE MOTION PASSED UNANIMOUSLY.

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

DR. PAMELA VINCENT, a representative Reckitt Benckiser Pharmaceuticals, discussed the recent changes in the prescribing information, dosage, and administration of Naloxone Sublingual Film. In the spring of this year, new indication was received for the initiation or abduction phase of opiate maintenance. This meant that patients can begin on the film product and continue treatment throughout the maintenance phase. This is for appropriate patients who are dependent on a short acting opiate i.e., prescription drug, street drug, or heroin. It does exclude long acting opiates if taken as indicated appropriately. Also, there is additional information added to the prescribing information regarding patients with hepatic impairment which can be contraindication for both moderate and severe hepatic impairment. There was additional wording regarding pregnancy added that it is Pregnancy Category C as it had been. The risk versus benefit wording has not really changed, and there is a short statement indicating that it may be associated with fetal harm, but no well controlled studies.

Dr. Balogun gave the Magellan presentation of Opiate Dependence Treatments. The agents in this class are indicated for treatment of opiate dependence, and have the mechanism of action of the new opioid receptor. Buprenorphine is a partial agonist, Naloxone is an antagonist, and Naltrexone is an opioid antagonist with the highest affinity of the mu opioid receptor. All agents in this class are Pregnancy Category C.

The utilization within this class was 594 claims in September 2014. The significant changes are that Evzio is a new medication in this class, and is a hand-held auto-inject formulation of Naloxone, which was approved by the FDA in April 2014. It is indicated for emergency treatment of opioid overdose, either known or suspected, as demonstrated by respiratory and/or central nervous system depression. It is not intended as a substitute for emergency medical care but for immediate administration for when opioids may have been used. It is classified as Pregnancy Category B.

Another new medication in this class is Bunavil which is a combination of buprenorphine and naloxone. It is a partial opioid agonist containing a fixed dose of buprenorphine and naloxone. It was approved June 2014. It is indicated for the maintenance treatment of opioid dependence, and should be used by patients who have been initially inducted using buprenorphine sublingual tablets. It is Pregnancy Category C, and there are no published comparative efficacy trials for Bunival versus Suboxone. There are also no significant clinical differences between Bunival and all the combination products that have both ingredients.

At the last review, a motion for therapeutic alternatives passed with two opposed.

Dr. Hope explained, for the record, that neither Evizo nor Bunavil is going to be part of the motion. Both came on the market after the last update and are not included in the packet. The new product in the packet that prompted it to be in this category is Zubsolv. The information

about Evizo and Bunavil is relevant information but not subject to the review. Evizo is completely different and is for overdoses and is not an opiate dependent drug. Unless some rebate issue going on with Magellan, it will not be part of this in the future.

Dr. Demain inquired if it was routine for patients that are on high dose long-acting narcotics to have an antagonist or reversal agent. Dr. Hope responded that that issue is a big topic on the national level right now. Some states are opening the door, and some states are not. Alaska is at the point where there is not a unified DHSS approach to it, and is currently on the prior authorization at the moment. There are providers out there that are preparing kits themselves with the ampules and a syringe. There are a number of approaches to this.

Dr. Demain stated that there are some drugs that patients are required to have at home such as epinephrine, and it seems like this would fall under the same guidelines. Dr. Carlson explained that it may be theoretically in the same concept, but someone who is on long-term agonist opiate treatment should have their dose stabilized such that they are no where near the point of respiratory depression and should almost never have need of any reversal treatment. Dr. Hope explained that the majority of conversations have revolved around heroin or recreational abuse. The FDA approval was sought for instances like when a child unintentionally takes drugs. The recreational use is what is really driving the market. In response to a question, Dr. Hope responded that Vivitrol is moving to preferred on the new list. Naltrexone oral does not require prior authorization, but is also not part of the review against these products. It was taken off prior authorization about two years ago. It was initially on prior authorization with the concern that the utilization would grow dramatically if the PA was removed, but that has not happened.

MR. O'RILEY MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

6. Re-Review of Anticonvulsants (Red Class)

DR. DAVID CHAPMAN, a representative of UCB, discussed Vimpat or lacosamide. It is a schedule 5 product and indicated in patients 17 years or older with partial onset seizures as mono-therapy or adjunctive therapy. Despite the availability of anti-epileptic drugs with various mechanisms of action, approximately 20%-40% of partial onset seizure patients are refractory to treatment or experience intolerable side effects. As shown in the prescribing information, Vimpat has been created as advocacy as adjunctive or mono-treatment in controlled pivotal studies in adult epilepsy partial onset seizure patients, with or without secondary generalization. The most common dose-related adverse events were dizziness, nausea, diplopia, and headache. Drug interaction studies in healthy volunteers showed no pharmacokinetic drug interaction with Vimpat and carbamazepine, valproate, digoxin, metformin, omeprazole, or warfarin. However, pharmacodynamic interaction cannot be ruled out. Vimpat is available in three formulations; a tablet, an oral solution, and an intravenous solution. No dosage adjustments are necessary when switching between the formulations. This allows for uninterrupted therapy in patients who may be hospitalized or unable to swallow oral tablets. Vimpat therapy can be initiated as a single loading dose in patients who require immediate anti-seizure medication such as patients experiencing break through partial onset seizures. In such cases, epilepsy patients receive the

therapeutic dose more rapidly than compared to standard titration. Caution is advised in patients with a known cardiac induction problem, those taking drugs known to induce PR interval prolongation, and patients with severe cardiac disease such as myocardio leukemia or heart failure. Additional warnings and precautions including suicidal behavior and ideation are included in the PI, which can be found at www.vimpat.com. In conclusion, Vimpat is available in three dosages formulations and can be administered at the loading dose. Also note, over 90% of Vimpat utilization is in patients with epilepsy. It is requested that access to this therapy be provided in the preferred position for appropriate adult Medicaid epilepsy patients in need of therapeutic options for partial onset seizures.

DR. KIM LOVEMEIR, a representative of Novium Pharmaceuticals, discussed the clinical and pharma-economic data for eslicarbazine or Aptiom. Aptiom is FDA approved for use as adjunct treatment of partial onset seizures in adults. Aptiom is not a controlled substance and it may be taken whole or crushed, with or without food. In the clinical trials that led to the FDA approval, patients had a median duration of epilepsy of nineteen years, with uncontrolled seizures despite one to three epilepsy medications, and were experiencing a median of eight seizures per month. Meta-analyses of these files showed patients demonstrated a significant reduction in standardized seizure frequency. The Aptiom label lists warnings for suicidal behavior and ideations and withdrawal seizures. Please refer to the full prescribing information for a complete list of warnings, precautions, and adverse events. While there are no head-to-head comparisons between different AEDs, a cost effectiveness model based on network analysis of Phase III, randomized controlled trials, with brand new AEDs for the treatment of partial onset seizures in adults, showed Aptiom to be cost effective on a cost per seizure avoided basis, and at a cost-per-response month basis for efficacy comparable to Keppra XR and greater than Vimpat. When highest and lowest doses for each of the comparators were evaluated separately, Aptiom showed the second highest efficacy among the low dose formulations and the highest efficacy among the highest dose formulations. In addition, Aptiom 800 mg. are the second lowest discontinuation rate, while Aptiom 1200 mg. had the second highest discontinuation rate. When three year effectiveness was evaluated for the highest and lowest doses in the cost effective model, Aptiom was cost effective relative to other brand name comparators and provided the highest number of seizures avoided in both scenarios. In closing, Aptiom has demonstrated efficacy in refracted partial onset seizure patients, and respectfully ask that Aptiom be added to the preferred drug list for Medicaid beneficiaries of Alaska.

Dr. Balogun gave the Magellan presentation of anticonvulsants. Agents in the anticonvulsant drug class have various indications including seizure disorders, neuropathic pain, migraine prophylaxis, and bipolar disorder. Anticonvulsants have very little or no direct comparative data in the treatment of seizures or any other indications. Selection of drugs for epilepsy treatment frequently depends on particular indications. Pregnancy categories for these agents vary between C and D, except valproates, which are classified as Pregnancy Category X. The elderly population required special considerations related to medications selection and dosage due to age related factors and their utilization of multiple medications for co-morbidities. Many drug interactions exist for the anticonvulsants including interactions among adjunctive anticonvulsants. There are small amounts of comparative data but extensive clinical trials between the agents have not been done. Overall, the agents have similar efficacy with the newer drugs having fewer serious adverse effects and drug interactions.

Utilization for this class was 3,990 claims in September 2014. Significant changes include there were five new drugs added to this class - Aptiom, Trokendi XR, Fycompa, Qudexy XR, and Oxtellar XR. Aptiom was approved in November 2013 and indicated for use in partial seizure disorders. It is a voltage-gated sodium channel blocker. The safety and effectiveness has not been established in patients below age 18. It is categorized as Pregnancy Category C. Serious dermatologic reactions have been reported with its use. Patients with prior dermatology reactions with oxcarbazepine should not be treated with Aptiom. Its clearance is decreased in patients with impaired renal function.

Trokendi XR was approved by the FDA in August 2013 and it is indicated for use in partial seizures, tonic-clonic seizures, and Lennox-Gastaut syndrome. It exhibits sodium channel blocking actions, and it potentiates the activity of GABA. It antagonizes the glutamate receptor and inhibits carbonic anhydrase. This medication is contraindicated in patients who have consumed alcohol within six hours before and/or after the dose due to a significant alteration in topiramate release from the capsules. It is classified as Pregnancy Category D.

Qudexy XR was approved by FDA in March 2014, and it the same mechanism of action and indications as Trokendi XR. It is contraindicated in patients with metabolic acidosis who are also taking concomitant metformin. It is also classified as Pregnancy Category D.

Fycompa is indicated for use as an adjunctive therapy for the treatment of partial seizures in children at least 12 years of age with epilepsy. Its use in children less than 12 years of age has not been established. It carries a black box warning for serious psychiatric and behavioral reactions. Fycompa may also cause certain neurologic effects including gait disturbances, dizziness, and somnolence.

At the last review, a motion for therapeutic alternatives passed unanimously.

Dr. Hope explained that it can be said that some of these medications are not being used as anticonvulsants, but they get lumped together based on their approval. With some of these drugs, we understand that the vast majority are not used for anticonvulsants.

MR. RILEY MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY MS. RADAR. THE MOTION PASSES UNANIMOUSLY.

7. Re-Review of Antidepressants - Other (Red Class)

There were no public testimonies.

Dr. Balogun gave the Magellan presentation on Antidepressants - Other. The drugs in this class either inhibit the re-uptake or block the receptors of transmitters such as dopamine, serotonin, and norepinephrine. Each of the drugs has a potential in the treatment of major depressive disorder. Patients failing to respond to one type of antidepressant may respond to another with a different mechanism of action or combination of both. Data showing superiority in efficacy of

one or another class of drugs are not robust or clinically meaningful. The agents in this class do differ in their adverse event profiles. When choosing therapy, include drug interaction profiles, pharmacokinetics, patient preference, and historical patient response. Utilization for this class was 2,413 claims in September 2104. The significant changes since last review include three new drugs, Fetzima, Brintellix, and Forfivo XL.

Fetzima is indicated for major depressive disorder, and is contraindicated within fourteen days of an MAOI or in a patient being treated with linezolid or intravenous methylene blue. Blood pressure and heart rate should be monitored prior to and during therapy because this medication has been reported to cause their increase. Also, because Fetzima has been reported to increase hepatic transaminases and cause fulminant hepatitis, this agent should be avoided in patients with a history of substantial alcohol use or chronic liver disease. It is classified as Pregnancy Category C. The most common adverse events include nausea, constipation, heart rate increase, and erectile dysfunction. Erectile dysfunction and urinary retention appear to be dose related. Limited comparative data was available.

Brintellix is indicated also for major depressive disorder. It is classified as Pregnancy Category C. It is also contraindicated within 21 days of using an MAOI or in a patient being treated with linezolid or intravenous methylene blue. The most common adverse reactions are nausea, constipation, and vomiting. Initiation is associated with high rates of nausea, which appear and dissipate after a medium of two weeks of therapy. There is limited comparative data.

Forfivo XL is classified as Pregnancy Category C. It is contraindicated in patients with a seizure disorder, anorexia and/or bulimia, or undergoing abrupt discontinuation of alcohol or sedatives. It is extensively metabolized in the liver, to active metabolites, which are further metabolized and excreted by the kidney. It is not recommended for use in patients with renal or hepatic impairments. There are no separate independent clinical trials available to establish the efficacy of this medication. Its efficacy in the treatment of major depressive disorder was determined from previous trials of the immediate-release formulation of bupropion, as well as data demonstrating bioequivalence of this specific formulation to other extended-release formulations.

At the last review, a motion for therapeutic alternatives passed unanimously.

Dr. Phillips stated that while she didn't have a lot of experience with the new drugs, when she did research on it, didn't see where there was that much difference. It would be helpful to hear from the other psychiatrists.

Dr. Hope explained that how a drug gets placed in what category depends on the bids, and what it is being compared against for the financials. There is a large amount of overlap. Dr. Bergeson stated that trazadone is not usually used for depression, but for sleep.

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

8. Re-Review of Antidepressants – SSRI (Red Class)

There were no public testimonies.

Dr. Hope explained the reason between a red and blue class was hard to determine. With the more robust program, it was felt that it was more understandable to combine to be either red or green. There is no blue this time and all were called red.

Dr. Balogun gave the Magellan presentation on Antidepressants – SSRI. SSRI's are antidepressants that block the reuptake of serotonin. Drugs in this class have varying FDA approved indications. They cause papillary dilation which may trigger an angle closure glaucoma attack in patients with anatomically narrow angles who do not have a patent iridectomy. The labels of most antidepressants include this warning.

Utilization for this class was 3,444 claims in September 2014. Significant changes since last review include a new drug in this class called Brisdelle. It is a 7.5 mg paroxetine capsule. It is not indicated for the treatment of any psychiatric condition, rather it is indicated for the treatment of vasomotor symptoms associated with menopause. It is the only SSRI indicated for this. Brisdelle is classified as Pregnancy Category X. If stopped abruptly, it can cause discontinuation symptoms.

The other significant change is that fluoxetine is indicated in combination with olanzapine for the treatment of depressive episodes associated with bipolar I disorder.

At the last review, a motion for class effect passed unanimously.

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

9. Re-review of Antipsychotics - Atypical (Red Class)

DR. KAREN WYNN, a representative with Forest, discussed Saphris. Schizophrenia and bipolar disorder are among the most complex and challenging conditions to manage. Both conditions are characterized by considerable symptoms, varying medication response rates, frequent medication switching, and medication non-compliance, which can potentially lead to high rates of relapse and hospitalization. According to the Agency for Health Research and Quality, the two conditions in 2011 with the largest numbers of readmissions for Medicaid patients were mood disorders and schizophrenia. These two conditions resulted in about \$588 million in hospital costs for the Medicaid population. These high re-admission rates suggest that there is still a significant unmet need for safe and effective therapy for treating these conditions. Saphris serves to broaden the amount of agents available to manage these conditions and Saphris is indicated for the acute and maintenance treatment of schizophrenia as well as the acute treatment of manic or mixed episodes associated with bipolar I disorder, both with mono therapy and as adjunct with lithium or valproate. Saphris is available as a rapidly dissolving sublingual tablet. It is also now available only in a black cherry flavor, which is more palatable than prior

formulations. The efficacy for the treatment of acute schizophrenia was established in two short-term placebo controlled trials while maintenance of effect was demonstrated in a long-term trial in which Saphris was significantly superior to placebo in preventing relapse of schizophrenia. Efficacy in the treatment of acute mania in bipolar I disorder was established in two short monotherapy trials, which demonstrated that Saphris exhibited clinically significant improvement in symptoms that occurred as early as day two, and continued until the end of the trial. Efficacy in the treatment of acute mania was also demonstrated in one adjunctive trial with lithium or valproate. Saphris carries a box warning associated with dementia related psychosis which applies to all agents in this class. For forewarnings and precautions, please see the prescribing information. Saphris has also been shown to have limited effects on prolactin, lipid, glucose parameters, and weight gain. It appears to have a favorable weight gain profile. This is confirmed in meta-analyses of seventeen clinical trials recently published in the Journal of Clinical Psychiatry. This potentially reduced metabolic impact is a favorable characteristic in a medication class that requires monitoring for such affects as recommended by the Hetis 2014 quality measures. Recently, the results of a retrospective analysis of claims data from 24 State Medicaid programs revealed that applied formulary restrictions to the atypical anti-psychotics was associated with higher total health care costs at the expense of modest savings in medication costs. Forest would like to request that Saphris be available to these vulnerable patients, and is respectfully asking to maintain the preferred status of Saphris on the State Medicaid formulary based on this established efficacy, favorable safety profile, and unique dosage form.

DR. KIM LOVEMEIR, a representative of Novium Pharmaceuticals, discussed Latuda. Latuda is indicated for the treatment of schizophrenia and bipolar depression. It is the only agent in this class with an indication that both monotherapy and adjunctive therapy with lithium or valproate for the treatment of bipolar depression. It is the only atypical anti-psychotic, other than clozapine, with a Pregnancy Category B rating. The safety and efficacy of Latuda has been established in numerous clinical trials. In these trials, patients are not experiencing significant increases in cardio metabolic risk, which is an important consideration given patients with mental illness have high rates of diabetes, obesity, and cardiovascular risk. With regards to health economic outcomes, Latuda has also demonstrated top effectiveness for patients with schizophrenia and bipolar depression. In a twelve month head-to-head schizophrenia trial, comparing Latuda to Quetiapine XR, patients on Latuda experienced a 27% lower risk of relapse and 57% lower risk of re-hospitalization. This translates into economic benefits for Latuda patients experiencing less total direct health care costs as compared to patients on Quetiapine XR. In another real world analysis of a multi State Medicaid data base of schizophrenia patients, there was approximately a 50% decrease in both all costs and mental health hospitalizations in the six months following Latuda initiation as compared to the six months prior to Latuda use. As a reminder, Latuda belongs to a class of agents that carry a box warning for increased risk of mortality in elderly patients with dementia related psychosis, and increased risk of suicidal behavior in children, adolescents, and young adults taking antipsychotics. Please refer to the full prescribing information for a complete list of precautions. In conclusion, patients with serious mental illnesses such as schizophrenia and bipolar disorder experience high levels of disability and are extensive users of resources. Latuda is a safe and cost effective agent to manage the difficult to treat patients. Request that Medicaid patients with schizophrenia and bipolar depression be allowed unrestricted access to Latuda.

DR. AMY EVERETT, a representative of Otsuka, discussed Abilify Maintena. Abilify Maintena as an injectable suspension is an atypical antipsychotic indicated for the treatment of schizophrenia. The efficacy of Abilify Maintena in adult patients for treatment of schizophrenia was demonstrated in a randomized trial, double blind placebo controlled trial in adults. Compared to placebo, Maintena showed a statistically significantly longer time to relapse, which was a primary end point. The secondary end point was a percentage of patients meeting relapse criteria was also significantly lower with the Maintena versus placebo. The safety profile of Maintena is expected to be similar to oral aripiprazole. Based on five placebo controlled trials where oral aripiprazole was given to adults with schizophrenia, discontinuation due to adverse events was 7% for oral aripiprazole, and 9% for placebo. Adverse reactions that led to discontinuation were similar for the two groups. The only common adverse reaction for oral aripiprazole in schizophrenia was acophesia. Abilify Maintena has a black box warning stating “elderly patients with dementia related psychosis treated with antipsychotics are at an increased risk of death compared to placebo”. Maintena is not approved for the treatment of patients with dementia related psychosis. For the complete box warning and additional safety information, please see the full PI. The mechanism of action of aripiprazole is unknown. It is proposed that the efficacy is mediated through its partial agonism at D2 and 5HT1A, and its antagonism in 5HT2A. Maintena is the first approved D2 partial anogist in a once monthly extended release injectable suspension. In a naturalistic setting, a phase three multi-center open label mirror image study in patients with schizophrenia was conducted to compare total psychiatric hospitalization rates between retrospective treatment with oral standard of care antipsychotics and prospective treatment with Maintena. 336 patients were part of the primary efficacy outcome comparison. After switching to Maintena, total psychiatric hospitalization rates were significantly lower compared with the standard of care period. Treatment emergent adverse events in patients included insomnia, acophesia, and psychotic disorder. Discontinuation due to adverse events during the prospective phase was 8.8%. Based on interim data from this mirror image study, Comat et al developed an economic model to estimate health care cost savings associated with Maintena treatment initiation among a subgroup of 76 patients who had at least one psychiatric hospitalization during the retrospective period prior to initiating Maintena. After switching to Maintena, total cost for patients with at least one hospitalization decreased 36% from \$36,000 to \$23,000. In closing, respectfully ask that Abilify Maintena be on the preferred drug list in the State of Alaska.

Dr. Balogun gave the Magellan presentation on Antipsychotics - Atypical. Agents in this class have varied indications that include schizophrenia, bipolar disorder, psychotic disorders, resistant depression, and irritability associated with autistic disorder. First generation antipsychotics exert their therapeutic effects primarily by blockade of the D2 receptors in the mesolimbic dopamine pathway. The blockade reduces the hyperactivity in this pathway and therefore, reduces the positive symptoms associated with psychosis. The second generation antipsychotics are serotonin-dopamine antagonists. Clinical properties that differentiate them from the first generation agents are their reduced incidence of EPS, potential increased efficacy for negative symptoms, and a decreased impact on prolactin levels. Clozapine and Latuda are Pregnancy Category B, and all other antipsychotics are Pregnancy Category C.

Injectable olanzapine requires the prescriber, pharmacy and patient, to be enrolled in the Zyprexa Relprevv Patient Care Program.

Utilization for this class was 3,584 claims in September 2014. Significant changes since last review include an addition of a drug, Versacloz. It is indicated for resistance schizophrenia, schizophrenia associated suicide prevention, and adjunctive therapy for depression. It is classified as Pregnancy Category B. Due to the risk of agranulocytosis, it is available only through a restricted program called the Versacloz Patient Registry, where prescribers, patients, and pharmacies must enroll.

At the last review, a motion that drugs in the oral preparation class with therapeutic equivalence and to include one first and one second generation injectable passed unanimously.

Dr. Hope stated that we are not looking at the first generation, but looking at the second generation here.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE ONE ORAL SOLUTION PRODUCT AND ONE LONG ACTING INJECTABLE PRODUCT, NOT ZYPREXA RELPREVV. SECONDED BY MS. RADAR.

In response to Dr. Demain's question about grandfather clauses when there is a product shift, Dr. Hope explained that the way our PDL is structured, it's a soft edit so they can still bypass it at the pharmacy with medically necessary documentation at the point of sale. When we look at these motions, we also take into account the utilization and the likelihood of the impact. Dr. Phillips stated that if a person is doing well on a particular drug, if it is not on the list, a hard edit or prior authorization will be done, because it is so hard to find something that works, and a person won't change it just because the medication has changed from a preferred to a non-preferred.

Mr. Hope explained that the hard edits used with this class, with that exact scenario, is that recipients are limited to one antipsychotic. If more than one is needed, then there is a hard edit. In response to Dr. Bergeson's comment about the difficulty in giving the meds to children as only one pill is allowed per day, Mr. Hope explained that with the pricing structure on different medications, when the 5 mg tablet costs the same as a 10 mg tablet, we have to address that.

MOTION PASSED UNANIMOUSLY.

10. Re-review of Sedative/Hypnotic (Red Class)

There were no public testimonies.

Dr. Balogun gave the Magellan presentation on Sedative/Hypnotic. Insomnia is commonly divided into three types based on duration; transient, short term, and chronic. The selection of a specific hypnotic is based in large part on whether the patient has problems with initiation or maintenance of sleep, co-morbid conditions, side effect tolerance, and availability. Sedative hypnotics should be prescribed at the lowest dose that treats the patient's symptoms. Drugs in

this class should be used with caution in patients receiving CNS depressants as the effects may be additive.

Utilization for this class was 785 in September 2014. Significant changes include an addition of a drug Hetlioz, which was approved January 2014. This agent involves the control of circadian rhythms. Because of individual differences in circadian rhythms, drug effects may not occur for weeks or months. This medication has not been studied in subjects with severe sleep apnea or severe COPD, or patients with severe hepatic impairment. Therefore, it is not recommended for these populations. It is classified as Pregnancy Category C and the indications include non-24 hour sleep/wake disorder in totally blind patients.

At the last review, a motion for therapeutic alternatives passed unanimously.

Mr. Hope explained that the list may have not been updated since Lunesta went generic, or it could be that there was no utilization. In response to Dr. Phillips question about whether the new drug, Hetlioz, belongs here, as it seems to be a different mechanism and it targets a specific population, Dr. Balogun explained it is only for totally blind patients and was classified based on the indication with it helping them to regulate sleep.

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

11. Review of Hypoglycemics, SGLT2 Inhibitors (Red Class)

DR. BOB SNEDIKER, a representative from Johnson and Johnson, discussed Invokana. Invokana is a unique product in that it is a sodium-glucose cotransporter inhibitor. A transporter is responsible for re-absorption of glucose in the kidney. By blocking this transporter, one effectively increases urinary glucose excretion, upwards of 100 grams per day, and works nicely with effects on weight and blood pressure. By increasing the glucose excretion in the urine, one can change the renal threshold for glucose excretion, and as a result, one will get reasonable reduction in hemoglobin A1C, blood pressure, and weight. The clinical data shows nine pivotal trials in phase III development, involving approximately 10,000 patients, who were studied in monotherapy add on to metformin, in dual therapy and triple therapy with add on to metformin and sulfonylurea. The A1C reduction across most of these studies is about 1%, which is a meaningful end point. The most compelling data is in two trials where we compared the Invokana 100 mg and 300 mg doses to cidiglipdon 100 mg per day or in combination with metformin versus glimeporide. In both those trials, the 300 mg dose of Invokana demonstrated statistically superior reduction of A1C versus both the cidiglipdon and glimeporide. Additionally, some of the key secondary end points of weight loss and lowering blood pressure add into the overall attractiveness of this product. From a safety standpoint, the most common side effects are primarily related to genital mycotic infections, which can be troublesome. Some studies show that the increase in health care resource utilization secondary to that side effect is minimal at best. One needs to maintain some degree of caution in patients with moderate renal impairment, as the efficacy of the drug is directly related to the integrity of the kidney. The

value of this product is a new mechanism of action, 1% lowering of hemoglobin A1C, lowering of blood pressure and weight loss.

Dr. Balogun gave the Magellan presentation on Hypoglycemics, SGLT2 Inhibitors. There are several pathways by which blood glucose is regulated in diabetic patients. The SGLT2 agents reduce renal glucose re-absorption in the proximal convoluted tubule, leading to increased urinary glucose excretion. There have been no clinical studies that have established conclusive evidence of macro vascular risk reduction with the use of these agents. The AACE guidelines for 2013 suggest that these agents are a 5th, 4th and 3rd choice in mono therapy, dual therapy, and triple therapy respectfully. The advice is that used these agents with caution, and acknowledges that their place in therapy for diabetic management remains undefined due to lack of experience with them. These drugs will likely be used as add-on therapy to two or three other agents, including insulin, in patients who would benefit from weight loss. The single component agents are contraindicated in patients with severe renal impairment, end stage renal disease, and patients on dialysis. Metformin-containing products like Invokamet are contraindicated in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis. The label carries a black box warning that although rare, potentially fatal lactic acidosis can occur due to metformin therapy. This risk increases with renal or hepatic impairment, sepsis, dehydration, excessive alcohol intake, and acute congestive heart failure. The safety and efficacy of Invokana, Invokamet, and Farxiga have not been established in patients under age 18.

This class was not previously reviewed, and the agents in this class include Invokana, Farxiga, Jardiance, and Invokamet. Utilization for this class was 25 claims in September 2014.

MR. O'RILEY MOVED DRUGS IN THE CLASS WERE THERAPEUTIC EQUIVALENCE. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

12. Re-review of NSAIDs (Red Class)

Dr. Balogun gave the Magellan presentation on NSAIDs. NSAIDs are commonly used to treat rheumatoid arthritis, osteoarthritis, pain, and various etiologies. Both oral and topical NSAIDs work by blocking COX-1 and COX-2 enzymes that catalyze the synthesis of prostaglandins from arachidonic acid, which are partially responsible for the development of pain and inflammation. NSAIDs are associated with adverse effects including GI bleeding, peptic ulcer disease, hypertension, edema, and renal disease. In addition, NSAIDs are linked to an increased risk of MI, which is reflected in the black box warning of all NSAIDs. They are contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft surgery. Elderly patients are at greater risk for serious GI events.

Utilization for this class was 3,175 claims in September 2014. Significant changes include an addition of Zorvolex to this class. Zorvolex is a low dose diclofenac formulation and contains diclofenac free acid whereas other diclofenac products contain a salt of it. Zorvolex has a reduced particle size which increases its surface area, leading to faster dissolution and absorption of the drug. It is indicated for mild to moderate pain and osteoarthritis. It is classified as Pregnancy Category C for patients less than 30 week gestation, and Category D for patients

starting at 30 week gestation. Safety and efficacy has not been established in patients less than 18 years of age.

At the last review, a motion for class effect to include COX-2 and a topical patch passed with one opposed.

Mr. Hope explained that meloxicam is counted as a COX-2. Dr. Demain commented that the main purpose of a COX-2 was because of a group of patients with aspirin sensitivity and NSAID sensitivity, and in addition, potentially improved GI side effect profiles. We can use medically necessary categories, and wanted to clarify why that is there. Mr. Hope stated that in the past, this was a COX-2 packet, and at that time Celebrex and Mobic were the two remaining. The packet has been shuffled from a COX-2 packet to a NSAID packet.

The patent for Celebrex expires December 31, 2014, and so this issue will likely be a moot point. Dr. Hope requested input regarding the COX-2 language. Dr. Demain explained that we have that category for a potential improvement in GI side effect profile or aspirin sensitivity. The meloxicam will not satisfy the second reason. It does satisfy the first. Don't see a problem with medical necessity. Mr. Hope requests clarity in the motion.

MR. RILEY MOVED FOR THERAPEUTIC ALTERNATIVES TO INCLUDE A TOPICAL AND CELECOXIB. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

Break from 9:33 a.m. to 9:47 a.m.

13. Re-review of Hypoglycemics, Incretin Mimetics/Enhancers (Green Class)

Dr. Balogun gave the Magellan presentation on Hypoglycemics, Incretin Mimetics/Enhancers. This class includes three subclasses; GLP-1 receptor agonist and DPP-4 inhibitors. GLP-1 receptor agonists increase insulin synthesis and release from pancreatic beta cells. They also lower glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production. The agents in this class are indicated for adjunct to diet and exercise to improve glycemic control in adults with Type II diabetes. The agents in this class have also been associated with acute pancreatitis, therefore patients should be observed for signs and symptoms of this. The agents are Byetta, Bydrucon, and Victoza. The second subclass is amylin analog and there is only one drug in this class. The agent is indicated as an adjunct therapy in Type I and Type II patients who use meal time insulin therapy and have failed to achieve desired glucose levels. The agent carries a black box warning for severe hypoglycemia associated with concomitant use of insulin. The third subclass is DPP-4 inhibitors. They are indicated as adjunct to diet and exercise to improve glycemic control in patients with Type II diabetes. They also increase insulin secretion and reduce glycogen, thereby lowering glucose levels. Concerns regarding the increased risk of pancreatitis and pancreatic cancers remain unresolved. No data is available for the use of these agents in pediatric patients.

Utilization for the class was 197 claims for September 2014, and this includes all three subclasses. At the last review, there were two motions. The first was to consider GLP-1 as a

class effect, and that passed unanimously. The second was to consider DPP-4 as a class effect to include Victoza and that passed unanimously.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE ONE GLP-1 AND ONE DPP-4. SECONDED BY MR. GREEAR. MOTION PASSES UNANIMOUSLY.

14. Re-review of Hypoglycemics, Insulin (Green Class)

Dr. Balogun gave the Magellan presentation on Hypoglycemics – Insulin. Exogenous insulin supplements deficient levels of endogenous insulin. These insulin products are utilized as replacement therapy in the management of both type I and type II diabetes. According to the American Association of Clinical Endocrinologists (AACE), when insulin therapy is indicated in patients with type II diabetes, therapy with long acting basal insulin analogues, which are glargine and detemir, should be the initial choice in most cases, as they are associated with less hypoglycemia. All insulin can cause a shift in potassium from the extracellular to intracellular space, so caution should be used in patients who are at risk for hypokalemia.

Utilization for this class was 825 claims in September 2014. This class was previously reviewed together, and at the last review, a motion for class effect to include at least one formulation from the long acting which includes 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, preferably including Lantus and it passed unanimously.

Mr. O’Riley stated that the current preferred list does not include a rapid acting pen. These are the ones just waiting for the new PDF to get updated.

MR. GREEAR MOVED A CLASS EFFECT TO INCLUDE AT LEAST ONE FORMULATION FROM THE LONG ACTING WHICH INCLUDES A PEN DELIVER SYSTEM, ONE FROM THE RAPID ACTING TO INCLUDE A PEN DELIVERY SYSTEM, INSULIN MIX, INSULIN 70/30, INSULIN N, AND INSULIN SUBGROUPS, PREFERABLY INCLUDING LANTUS. SECONDED BY MR. O’RILEY. MOTION PASSES UNANIMOUSLY.

15. Re-review of Hypoglycemics, Metformin (Green Class)

Dr. Balogun gave the Magellan presentation on Hypoglycemics, Metformin. Metformin decreases hepatic glucose production. It decreases intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Glyburide and glipizide lower blood glucose by stimulating the release of insulin from the pancreas. Metformin reduces A1C by 1.5-2 % and fasting plasma glucose levels by about 20%.

Utilization for this class was 1,231 claims for September 2014. At the last review, a motion for class effect passed unanimously.

MR. O'RILEY MOVED THAT A CLASS EFFECT. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

16. Re-review of Hypoglycemics, TZDs (Green Class)

Dr. Balogun gave the Magellan presentation on Hypoglycemics, TZDs. The TZDs work by decreasing insulin resistance. Combination products are available and may improve adherence for patients requiring combination therapy. In 2011, due to elevated risk of cardiovascular events, use of Avandia and products containing Avandia were significantly restricted. However, in November 2013 after further review of the data, the FDA found that the evidence of the increased risk of heart attack or death in patients treated with these products were lacking and removed the prescribers and distributors restrictions.

Utilization for this class was 113 claims for September 2014. At the last review, a motion for therapeutic alternatives passed unanimously.

Dr. Hope stated that there was a reason for putting this on the agenda, but can't remember what it was, and will review to make sure there is a reason to continue reviewing this for future meetings.

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

17. Re-review of Neuropathic Pain (Green Class)

Dr. Balogun gave the Magellan presentation for Neuropathic Pain. Neuropathic pain can be caused by a number of different diseases. Limited comparative head to head data exists on neuropathic pain and various professional guidelines suggest different first line and second line treatments based on indication. When selecting a drug, consideration should be given to other factors such as adverse event profiles, ability to treat co-morbidity, drug to drug interactions, and contraindication. This class includes agents with indication for post-herpetic neuralgia, diabetic peripheral neuropathy, neuropathic pain in general, and fibromyalgia. The administration varies from topical to oral. For the indication of neuropathic pain, the safety and effectiveness of these agents in children have not been adequately studied.

Utilization for this class was 2,229 claims for September 2014. At the last review, the motion for therapeutic alternatives passed unanimously.

MR. O'RILEY MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

18. Re-review of Antifungals, oral (Green Class)

This item has been moved to the January agenda.

19. Re-review of Stimulants and Related Agents (Green Class)

Dr. Balogun gave the Magellan presentation on Stimulants and related agents. The most common use of stimulants is for the treatment of ADHD for which they are considered first-line therapy. All the indications include hyper somnolence and obesity. Stimulants act by blocking the reuptake of norepinephrine and dopamine into the presynaptic neuron and increasing their release into the extraneuronal space. All stimulants used to treat ADHD are associated with peripheral vasculopathy. Signs and symptoms generally improve after reduction in dose or discontinuation of the drug. Monitor for digital changes during treatment for ADHD stimulants is recommended.

Utilization for this class was 2,604 claims in September 2014. At the last review, a motion for therapeutic alternatives to include at least one extended release and one non-stimulant formulation passed unanimously. Dr. Hope stated that recently the FDA has tagged two of the generics for Concerta as being non-AB rated anymore because of bioequivalent issues. Dr. Bergeson explained that this is a non-issue for the prescriber because when treating, just go to the higher dose.

MR. O'RILEY 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. BERGESON.

Dr. Hope clarified that the intent of this motion is to have an alpha agonist, the intent is to also have a non-stimulant, non alpha agonist, and the intent is to also have a long acting stimulant. The intent is to not use the alpha agonist as the non-stimulant to cover both.

THE MOTION PASSED UNANIMOUSLY.

20. Review minutes from September 19, 2013 meeting

Dr. Hope explained that the minutes were reviewed, and there were no changes other than there were several places in the motions where the person who seconded the motion was not identified by name. Suggest that a note just be made that it was seconded by name unavailable.

Without objection, the minutes of September 19, 2014 were approved.

21. Comments from Committee Members or Chair

1. The new phone set up worked much better for this meeting, and work to improve the phone system will continue.
2. The next meeting date is in January.
3. Julie Pritchard was thanked for her years of service and wished good luck.

22. Adjourn

Without objection, the meeting adjourned at 10:15 a.m.