ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

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

MINUTES OF MEETING
November 15, 2019
8:00 a.m.

Committee Members Present:
Ryan Ruggles, PharmD, Acting Chair
Robert Carlson, MD (telephonic)
Vincent Greear, R.Ph. (telephonic)
Sarah Doran-Atchison, PharmD (telephonic)
Claudia Phillips, MD (telephonic)
John Riley, PA
Trish White, R.Ph. (telephonic)

Committee Members Absent:
Jeanna Hiestand, MD (excused)
Diane Liljegren, MD
Charles Ryan, MD

Others Present:
Erin Narus, PharmD, R.Ph., State of Alaska
Charles Semling, PharmD, R.Ph.
Marti Padilla, R.Ph., Magellan Medical Administration
Umang Patel, Pharm D, R.Ph., Magellan Medical Administration
Betty Caudle, Kron Associates

1. Call to Order – Chair

Dr. Ruggles called the meeting to order at 8:01 a.m. At this meeting, Magellan will give their presentation first and then industry will speak in an attempt to streamline the meeting.

2. Roll Call

The roll call was taken, and a quorum was present.

3. Public Comments - Local Public/Health Practitioners

There were no local public/health practitioner comments.

4. Class Review, Discussion & Vote

4-A. Cystic Fibrosis: CFTR Potentiator Agents (Blue Class); Antibiotics, Inhaled (Blue Class); Pancreatic Enzymes (Green Class)

Cystic Fibrosis: CFTR Potentiator Agents (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Cystic Fibrosis: CFTR Potentiator Agents. Cystic fibrosis is a serious autosomal recessive multiorgan disorder. It affects approximately 30,000 children and adults in the U.S. and is the most common fatal genetic disease in Caucasians. Children are anticipated to live to approximately 40 years of age with current treatments. In 2017, adults comprised approximately 53.5% of the CF population; whereas in 1987, they comprised approximately 30%. Mutations lead to the disease of the exocrine gland function, resulting in the formation of thick mucus that builds up in the lungs, digestive tract, and other parts of the body. The CF transmembrane conductance regulator (CFTR) functions as a chloride channel. Mutations in CFTR results in abnormalities of chloride transport across epithelial cells on mucosal surfaces. The goals of treatment are primarily threefold: maintaining lung function by controlling injection and clearing mucus in the airway; maintaining appropriate growth by providing nutritional support; and managing disease complications. There are no new changes in the guidelines since last year.

Symdeko is a combination of Tezacftor and Ivacaftor. In June 2019, the FDA expanded approval of Symdeko to include pediatric patients age 6 years of age and older with cystic fibrosis who have certain genetic mutations; previously, it was approved only in patients 12 years of age and older. Dosage recommendations were reviewed. All doses should be administered with fat-containing food. It is available in a tablet formulation.

Kalydeco was approved by the FDA in May 2019 with an expanded indication for use in patients as young as 6 months to 11 years of age who have one CFTR gene mutation that is responsive to Ivacaftor potentiation based on clinical and/or in vitro assay data. Dosage recommendations were reviewed. It is available in a tablet formulation and unit-dose oral granule packets.

Trikafta was approved by the FDA in October 2019. It is indicated for the treatment of CF in patients ages 12 years of age and older who have at least one F508del mutation in the CFTR gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one F508del mutation. It should not be used in patients with severe hepatic impairment. It is not recommended in patients with moderate hepatic impairment unless the benefit exceeds the risk. Liver function tests should be assessed prior to initiating, every three months during the first year of treatment, and annually thereafter. In terms of pregnancy, there are limited and incomplete human data from clinical trials. It has not been studied in patients with severe or end-stage renal disease, but it is recommended to use with caution. For patients with mild or moderate renal impairment, there is no dosage adjustment recommended. Dosage recommendations were reviewed. It is available in a tablet formulation.

The utilization report was reviewed and 100% of the prescriptions were for preferred products.

Dr. Semling noted that Dr. Dion Roberts, an expert in cystic fibrosis, was in favor of the inclusion of Trikafta on the PDL, as it has been shown to have better outcomes.

LISA ALLEN, a representative of Vertex, discussed Trikafta, a combination of Elexacaftor, Tezacaftor and Ivacaftor that was approved by the FDA on October 21, 2019, for patients with cystic fibrosis, age 12 years and older, who have at least one F508del mutation in the CFTR gene. Trikafta works by targeting the underlying cause of cystic fibrosis, which is a defect in the CFTR protein. The objectives of cystic fibrosis care include, but are not limited to, preserving lung function, optimizing nutritional status, and overall improvement of respiratory manifestations including pulmonary exacerbations. Several trials and their outcomes were reviewed.

Dr. Umang Patel noted that at the last review, a motion for therapeutic alternatives, to be used appropriately, passed unanimously.

DR. CARLSON MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, TO BE USED APPROPRIATELY. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

Cystic Fibrosis: Antibiotics, Inhaled (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Cystic Fibrosis: Antibiotics, Inhaled. This class now includes mycobacterium avium complex (MAC) lung disease. It is the most common nontuberculous mycobacterial (NTM) lung infection. Treatment is continued until sputum cultures are consecutively negative for at least 12 months; typical duration exceeds 18 months. Eradication is difficult, and recurrence and relapse are common. The timing of treatment depends on the type of disease and the risk of progression. While fibro cavitary disease has a rapid progression and warrants prompt treatment, a course of observation may be reasonable for patients with nodular bronchiectasis disease, if the patient has minimal symptoms or radiographic findings, or the patient has comorbid conditions that are considered to be more serious than the MAC lung infection. During observation, sputum cultures are generally monitored every two to three months, and repeat imaging occurs after approximately six months. Signs of disease progression indicate the need to antibiotic therapy.

The guidelines from the American Thoracic Society (ATS) and Infectious Diseases Society of America, the Cystic Fibrosis Foundation (CFF) and European Cystic Fibrosis Society (CFS) were reviewed.

Arikayce is the first FDA-approved inhaled antibiotic to be used in the treatment of refractory MAC as a part of a combination antibacterial drug regimen. It is contraindicated in patients with a known aminoglycoside hypersensitivity. Aminoglycoside use, including Amikacin Liposome, can result in ototoxicity, nephrotoxicity, neuromuscular blockade, and bilateral congenital deafness in pediatric patients exposed in utero. Dosage recommendations were reviewed. It is available as an inhalation suspension.

The utilization report was reviewed and 100% of the prescriptions were for preferred products.

There were no industry comments.

Dr. Umang Patel noted that at the last review, a motion for therapeutic alternatives passed unanimously.

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

Cystic Fibrosis: Pancreatic Enzymes (Green Class)

Dr. Umang Patel gave the Magellan presentation on Cystic Fibrosis: Pancreatic Enzymes. The utilization report was reviewed and 95% of the prescriptions were for preferred products. At the last review, a motion for therapeutic alternatives passed unanimously.

DR. GREEAR MOVED A CLASS EFFECT. SECONDED BY DR. PHILLIPS.

In response to Dr. Carlson, Erin Narus said when developing the PDL, staff would consider the motions as well as the conversations and concerns expressed during the discussion. Therapeutic alternatives mean there should be representation of alternative mechanism of action; whereas class effect means the mechanisms of action are essentially uniform.

THE MOTION PASSED UNANIMOUSLY.

4-B. Central Nervous System: Multiple Sclerosis Agents (Red Class); Stimulants and Related Agents (Red Class); Sedative Hypnotics (Blue Class); Anticonvulsants (Red Class); Antipsychotics - Atypical (Red Class); Antidepressants (Red Class); Alzheimer's Agents (Green Class)

Central Nervous System: Multiple Sclerosis Agents (Red Class)

Dr. Umang Patel gave the Magellan presentation on Central Nervous System: Multiple Sclerosis Agents. Multiple sclerosis (MS) is a complex human autoimmune-type inflammatory disease of the central nervous system. More than 2.3 million people worldwide have MS with 1 million in the U.S. MS occurs most commonly in whites, with rare cases in African-Americans and Asian-Americans. Although the etiology is predominately unknown, MS is characterized pathologically by demyelination and subsequent axonal degeneration. The nerve degeneration associated with MS can result in a wide variety of symptoms including sensory disturbances in the limbs; optic nerve dysfunction; ataxia; fatigue; and bladder, bowel, and sexual dysfunction. Severe cases may result in partial or complete paralysis. While cognitive impairment occurs in approximately 50% of people with MS, only 10% experience serious intellectual deterioration. MS can be categorized as either relapsing-remitting MS or primary progressive MS. Relapses or attacks typically present sub-acutely, with symptoms developing over hours to several days, persisting for several days or weeks, and then gradually dissipating. The clinical course of MS falls into one of the following categories, with the potential to progress from less severe to more serious types. Relapsing-remitting MS presents clearly defined, self-limited attacks of neurologic dysfunction, followed by periods of remission without disease progression. Most patients experience a recovery of function that is often, but not always, complete. Primary progressive MS presents nearly continuous worsening of disease not interrupted by distinct relapses; some of these individuals have occasional plateaus and temporary minor improvements. Secondary progressive MS presents relapsing-remitting disease course at onset, followed by progression with or without occasional relapses, minor remissions, and plateaus; most patients

eventually convert to progressive MS. Progress-relapsing MS presents progressive disease from onset, with clear, acute relapsing that may or may not resolve with full recovery; unlike relapsing-remitting MS, the periods between relapses are characterized by continuing disease progression. Clinically isolated syndromes present the first episode of neurologic symptoms due to inflammation or demyelination lasting at least 24 hours. Patients with MRI-detected brain lesions consistent with MS are at high risk of developing MS.

Mayzent was approved by the FDA in March 2019. It is indicated for relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease in adults. Adverse events may include an increase in blood pressure, macular edema, and transient bradycardia. It is contraindicated in patients with myocardial infarction, unstable angina, stroke or TIA, class III and IV heart failure, decompensated heart failure requiring hospitalization in the last six months. It is contraindicated in patients with CYP2C9*3/3 genotype. Dosage recommendations were reviewed. It is available as a tablet formulation. Mayzent's mechanism of action was reviewed. Human data of this medication in pregnancy are inadequate to advise a maternal or fetal risk; however, based on animal data, it may cause fetal harm. There is no dose adjustment needed in hepatic or renal impairment, but it has not been studied in patients with end-stage renal disease or hemodialysis.

Mavenclad was approved by the FDA in March 2019. It is indicated for relapsing forms of MS, including relapsing-remitting disease and active secondary progressive disease in adults. Due to its safety profile, the use of this medication should generally be reserved for patients who have had an inadequate response to or are unable to tolerate an alternative drug indicated for MS. Due to its safety profile, it is not recommended for patients with clinically isolated syndrome. It is contraindicated for patients with current malignancy, and it carries a boxed warning for increased risk of malignancy. It is contraindicated for women who are breastfeeding, within 10 days following the last dose, or are pregnant; and women and men of reproductive potential who do not plan to use effective contraception during the course of therapy; and for six months following the last dose in each treatment course. The labeling has a boxed warning for increased risk of teratogenicity. It is also contraindicated in patients with HIV or other active chronic infections as they are at an increased risk of infection. Dosage recommendations were reviewed. It is available in a tablet formulation. Mavenclad's mechanism of action was reviewed. There is no dose adjustment for patients with mild hepatic impairment, but it is not recommended for patients with moderate to severe hepatic impairment. Renal impairment may increase the concentration of this medication. No dosage adjustment is recommended in patients with mild renal impairment, but it is not recommended in those with moderate to severe renal impairment.

In 2018, the FDA sent out a communication on Lemtrada. Rare but serious cases of stroke and tears in the lining of arteries in the head and neck, which can lead to permanent disability and death, have occurred in patients with MS shortly after they received Lemtrada. A new warning about these risks were added to the PI and the medication guide, and the risk of stroke was added to the existing boxed warning. Health care practitioners should advise patients of this risk and recommend they seek out immediate medical attention if experiencing symptoms.

There were numerous indication updates for MS products. Ocrevus now reads for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease in adults; and primary progressive MS in adults. Rebif, Plegridy and Tecfidera had indication statement updates that read for the treatment of relapsing forms of MS to

include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease in adults. Copaxone, Tysabri and Avonex had indication statement updates that read for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease in adults. Betaseron and Extavia, consistent with other MS agent labeling revisions, had indication updates that read for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease.

The utilization report was reviewed and 79% of the prescriptions were for preferred products.

LINDA FINCH, a representative of Biogen, discussed Vumerity, a new oral medication for MS that was approved by the FDA last week. Vumerity's mechanism of action was reviewed. It has the same active metabolite as Dimethyl Fumarate, but it is a distinct chemical structure that offers a differentiated GI tolerability profile. It is indicated for the treatment of relapsing forms of MS including clinically isolated syndrome, relapsing-remitting disease, and active SPMS in adults. Several trials and their outcomes were reviewed. No serious opportunistic infections have been reported to date, but since it has the same active metabolite as Dimethyl Fumarate, it carries the same warnings and precautions. Patients treated with Vumerity experienced a 79.5% reduction in the risk of relapse. Vumerity offers efficacy similar to Tecfidera, but with a potentially improved GI tolerability profile. Please refer to the prescribing information for further information on the warnings and precautions.

MELISSA SOMMERS, a representative of Novartis, discussed Mayzent. There are 16 to 17 drugs in this class, but what makes Mayzent unique is that we conducted the largest ever clinical trial in secondary progressive MS patients. Although there is label harmonization, all agents have similar reading labels for this class. Data suggests that roughly 75% of SPMS patients are currently being treated, yet drugs other than Mayzent have tried and failed in this area. Several trials and their outcomes were reviewed. About 80% of patients using Mayzent will not require a first-dose observation. We request that Mayzent be retained on the PDL.

In response to Erin Narus, Ms. Sommers explained why the Mayzent trial was the only one with a positive outcome and noted that Tecfidera halted their SPMS trial prematurely.

Erin Narus encouraged the committee to review the actual clinical outcomes data for the trials to evaluate both the benefits and safety of the class.

SHIRLEY QUACH, a representative of Genentech, discussed Ocrevus. Current MS guidelines recommend early use of DMTs for the treatment of MS to prevent accumulation of disability and protect the patient's quality of life. Once a patient's disease progresses, they cannot get back what they have already lost. Ocrevus is approved for relapsing forms of MS. It is the first and only FDA approved agent for primary progressive MS. Several studies and their outcomes were reviewed. Ocrevus has been on the market since 2017. There is open label extension study out to years five and six. Long-term safety data continues to be consistent with clinical trials. Efficacy and safety data were submitted. Based on this data, we request that Ocrevus be added to the PDL because patients deserve the best possible treatment, as early as possible, to protect their quality of life.

LYNDA FINCH, a representative of Biogen who spoke earlier, discussed the SENTINEL trial for Tysabri and its outcomes. The trial was only for secondary progressive MS and did not include any

patients with active SPMS. The primary endpoint was negative, but there was a rigorous combined endpoint for the trial that was exploratory. The only reason the Tecfidera trial was stopped was we realized it was not the right endpoint to be looking at and was not achievable because of the stringency. However, we did see efficacy in one of the endpoints, the nine-hold peck test that demonstrates upper limb dexterity and mobility, and that was statistically significant and showed an improvement in patients with purely secondary progressive disease. The MASON trial enrolled active and non-active SPMS patients, but there was no statistically significant difference for patients with non-active SPMS.

Dr. Umang Patel noted that at the last review, a motion for therapeutic alternatives passed unanimously.

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

Central Nervous System: Stimulants and Related Agents (Red Class)

Dr. Umang Patel gave the Magellan presentation on Central Nervous System: Stimulants and Related Agents. Attention deficit hyperactivity disorder (ADHD) has been diagnosed in approximately 15% of children ages 4 to 17 and 4% of adults. It is a chronic condition with core symptoms of inattention, hyperactivity, and difficulty controlling behavior. It may also be accompanied by internalized disorders such as sadness and anxiety, as well as aggressive and oppositional disorders. The three main types of ADHD are primary hyperactive, primary inattentive, and mixed. Children with ADHD may experience academic underachievement, difficulties in personal relationships, and low self-esteem. Symptoms of ADHD tend to improve with age; however, this may be due in part to improved coping skills. The continuation of synaptogenesis and myelinization into adolescence and young adulthood, especially in the frontal lobes, may also play a role in the improvement of symptoms. One-third of children with ADHD will retain the diagnosis as they enter into adulthood.

Hypersomnolence, or excessive sleepiness, is a primary and often debilitating symptom experienced by patients with narcolepsy, obstructive sleep apnea-hypopnea syndrome (OSAHS), and shift work sleep disorder (SWSD). The defining characteristic of hypersomnolence is a consistent inability to stay awake and alert enough to safely and successfully accomplish tasks of daily living. Persons experiencing excessive sleepiness typically complain of fatigue, tiredness, lapses of attention, lack of energy, low motivation, difficulty concentrating, disruptive sleep, snoring, or difficulties at work.

While CPAP therapy has been shown to improve daytime sleepiness in patients with obstructive sleep apnea, the level of sleepiness does not always normalize. To address this residual daytime sleepiness, pharmacologic treatments may be beneficial. Medications such as modafinil, armodafinil, or Sunosi are FDA-approved for excessive daytime sleepiness associated with OSAHS. Modafinil and armodafinil are also indicated for sleep problems resulting from circadian rhythm disruption. These medications, along with CNS stimulants such as dextroamphetamine, methylphenidate, mixed amphetamine salts, and amphetamine sulfate tablets, are used for narcolepsy. The potential for adverse cardiovascular events with CNS stimulant use may be of concern, especially in this overall high-risk patient population. Due to their lack of sympathomimetic activity, modafinil and armodafinil are relatively free of adverse cardiovascular effects.

Sunosi was approved by the FDA in March 2019. It is indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea. Anxiety, insomnia, and irritability have been observed in clinical trials with Sunosi. It has not been evaluated in patients with psychosis or bipolar disorders and should be used with caution in these patients. Sunosi causes a dose-dependent increase in systolic blood pressure, diastolic blood pressure, and heart rate. The need for continued treatment with Sunosi should be reassessed periodically, and any patient who develops increased blood pressure or heart rate that is not controlled by a dose reduction of Sunosi or medical intervention should consider discontinuation of this medication. Drugs that increase levels of dopamine or bind directly to dopamine receptors may result in pharmacodynamic interactions with this medication. These interactions have not been evaluated; therefore, use caution when using Sunosi with any of those agents. Dosage recommendations were reviewed. It is available in a tablet formulation. Safety and efficacy have not been established in patients younger than 18 years of age. There is insufficient data available for patients who are pregnant. Dose adjustments are recommended for patients with moderate to severe renal impairment. It is not recommended for patients with end-stage renal disease.

Wakix was approved by the FDA in August 2019. It is indicated for the treatment of excessive daytime sleepiness in adult patients with narcolepsy. It is contraindicated in patients with severe hepatic impairment. It prolongs the QT interval, with a corrected QT increase of 4.2 milliseconds at the highest recommended dose. It should be avoided in patients with known QT prolongation or those using other medications that are known to prolong the QT interval. Wakix should be avoided in patients with a history of cardia arrhythmias or those at risk for torsade de pointe or sudden death. Hepatic or renal impairment may increase the risk of QT prolongation. Dosage recommendations were reviewed. It is available in a tablet formulation. It may take up to eight weeks for some patients to achieve a clinical response. It has not been established in patients younger than 18 years of age. There is limited data for patients who are pregnant to identify a drug-associated risk for miscarriage or major birth defects. It is contraindicated in patients with severe hepatic impairment. A dose adjustment and added monitoring is required for patients with moderate hepatic impairment. A dose adjustment is recommended for patients with moderate to severe renal impairment. It is not recommended in end-stage renal disease.

Adhansia XR was approved by the FDA for treatment of ADHD in patients 6 years of age and older. CNS stimulants have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy. It can cause an increase in blood pressure and heart rate. Monitor all patients for hypertension and tachycardia. Sudden death, stroke and myocardial infarction have occurred in adults treated with CNS stimulants. Avoid use in patients with structural cardia abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease, and other serious heart problems. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during treatment. Dosage recommendations were reviewed. It is available in a capsule formulation. It has not been assigned a pregnancy category in the FDA's revised pregnancy risk formatting. No dose adjustment is needed for renal or hepatic impairment.

Evekeo ODT was approved by the FDA for the treatment of ADHD in patients 6 to 17 years of age. It is contraindicated with use of monoamine oxidase inhibitor (MAOI) or within 14 days of MAOI dose. Sudden death, stroke and myocardial infarction have occurred in adults treated with CNS stimulant treatment. Dosage recommendations were reviewed. It is available as a tablet formulation.

The utilization report was reviewed and 98.6% of the prescriptions were for preferred products.

There were no industry comments.

Dr. Carlson noted that by combining adolescent ADD, adult ADD, daytime sleepiness and narcolepsy in the same category, the only option was therapeutic alternatives with modifications.

Dr. Ruggles noted that at the last review, a motion for therapeutic alternatives, to include at least one oral preparation, one extended release preparation, one non-stimulant preparation, one alpha agonist, and one orally disintegrating preparation or liquid, passed unanimously.

Dr. Phillips suggested that Magellan change the class. Dr. Ruggles noted that many of the drugs in the class have dual indications, which might make it difficult to separate the class. Dr. Greear noted that utilization in this class was 98% for preferred products. Dr. Semling noted that this class would also be reviewed by the DUR Committee.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, TO INCLUDE AT LEAST ONE ORAL PREPARATION, ONE EXTENDED RELEASE PREPARATION, ONE NON-STIMULANT PREPARATION, ONE ALPHA AGONIST, AND ONE ORALLY DISINTEGRATING PREPARATION OR LIQUID. SECONDED BY DR. GREEAR. THE MOTION PASSED UNANIMOUSLY.

Central Nervous System: Sedative Hypnotics (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Central Nervous System: Sedative Hypnotics. Insomnia is a complex symptom that comprises difficulty falling asleep, staying asleep, or non-refreshing sleep in combination with daytime dysfunction or distress. The symptom complex can be an independent disorder (primary insomnia) or the result of another condition (secondary insomnia). It is commonly divided into three types based on duration. Transient insomnia lasts up to one week and is often referred to as adjustment sleep disorder because it is often caused by acute situational stress, such as a test or deadline, and is recurrent with the same or similar stresses. The second type, short-term insomnia, lasts one to six months and is usually associated with more persistent stressful situational (death or illness) or environmental (noise) factors. Chronic insomnia is insomnia lasting more than six months. The incidence of insomnia in children ranges from 1% to 6%. In children with neurodevelopmental or psychiatric comorbidities, the incidence is as high as 50% to 75%. Insomnia in children may result in irritability, restlessness, lack of concentration, suicide risk, and poor memory.

Non-24-hour sleep-wake disorder (N24SWD or non-24) is a chronic circadian rhythm disorder that causes problems with the timing of sleep and sleep patterns. It occurs in approximately 55% to 70% of people who are completely blind but can also be experienced by sighted people. The condition is characterized by the failure of a person's biological clock to synchronize to a 24-hour day light-dark cycle. In people who are completely blind or have no perception of light, this is due to their eyes' inability to register light signals. In sighted people, N24SWD may be due to a number of factors such as altered sensitivity of light on circadian rhythm, self-selected changes in light exposure late in the day, and hormonal factors. Those with the disorder may have difficulty falling or staying asleep and may wake up feeling as if they need more rest. People with N24SWD may find their sleep patterns reserved. N24SWD onset most often occurs in late teen or early 20s but can occur at any age and appears to be a life-long effect.

The guidelines from the American Academy of Sleep Medicine (AASM), the American College of Physicians (ACP), and the National Sleep Foundation (NSF) were reviewed.

In 2019, the FDA required a boxed warning for serious injuries and death from complex sleep behaviors in patients taking eszopiclone, zaleplon, and zolpidem and a contraindication to avoid use in patients who have previously experienced an episode of complex sleep behavior with these agents.

The utilization report was reviewed and 68.2% of prescriptions were for preferred products.

There were no industry comments.

Dr. Umang Patel noted that at the last review, a motion for therapeutic alternatives passed unanimously.

Dr. Phillips questioned if a melatonin like drug should be included in the motion since it was not on the current PDL. Dr. Semling said the medically necessary clause could always be utilized. The committee discussed the utilization report and the prescriptions that were for non-preferred products.

Erin Narus noted that there were therapeutic alternatives within the class. The question for staff is whether the goal of the committee is to have additional mechanisms of action in the class that reflect what is being prescribed in the community or if there are different criteria.

Dr. Riley felt that the motion should include a melatonin like drug. Dr. Semling reiterated that the medically necessary clause could be utilized to prescribe non-PDL medications.

DR. GREEAR MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. CARLSON.

Dr. Phillips said she would support the motion but hoped staff would consider the committee's desire to have additional options.

THE MOTION PASSED UNANIMOUSLY.

Central Nervous System: Anticonvulsants (Red Class)

Dr. Umang Patel gave the Magellan presentation on Central Nervous System: Anticonvulsants. Epilepsy is one of the most common disorders of the central nervous system (CNS). It is defined when a person has two or more seizures. It affects 2.2 million Americans, with 150,000 new cases diagnosed each year. The risk is estimated to be 1% from birth to 20 years of age, and 3% at 75 years of age. Isolated seizures may also occur during a febrile illness, after head trauma, or as a result of withdrawal from alcohol or sedative/hypnotics. A seizure is traceable to an unstable cell membrane or cluster of cells. Excessive excitability spreads either locally (partial seizure) or more widely (generalized seizure). Partial seizures begin in one hemisphere of the brain and, unless they become secondarily generalized, they can cause alterations in motor functioning, sensory symptoms, or automatisms. If there is no loss of consciousness, they are called simple partial. If there is loss or impairment of consciousness, they are called complex partial. About 70% of patients with epilepsy can be maintained

on one drug. Noncompliance and evolving refractory epilepsy are common reasons for treatment failure. If control is not achieved with one drug, an alternative medication should be attempted before others are added to current therapy.

Lennox-Gastaut syndrome is one of the most severe forms of childhood epilepsy and one of the hardest to treat. It is characterized by mental retardation and multiple seizure types. Patients can have seizures daily, sometimes experiencing several seizures a day. Patients may also experience drop attacks, which are defined as a loss of muscle control causing the patient to fall abruptly to the floor.

Infantile spasm primarily consists of a sudden bending forward of the body with stiffening of the arms and legs. West syndrome is characterized by infantile spasms, developmental regression, and a specific pattern on electroencephalography (EEG) testing called hypsarrhythmia (chaotic brain waves). The onset is usually in the first year of life, typically between 4 and 8 months, usually stops at age 5, but may be replaced by other seizure types.

Dravet syndrome is a rare, catastrophic form of epilepsy that presents in the first year of life and is characterized by frequent, prolonged seizures. Patients may experience multiple seizure types during their lifetime. Infants often experience multiple comorbidities over their lifetime related to the persistent seizure activity, including behavioral and developmental delay. This syndrome is also associated with a 15% to 20% mortality rate due to Sudden Unexpected Death in Epilepsy (SUDEP).

The goal of treating epilepsy is to reduce the frequency of seizure occurrence along with providing the best possible quality of life. Treatment will depend on the type of seizures. Many different classes of drugs are available, and some patients will require more than one drug to control their seizures.

The guidelines from the American Epilepsy Society (AES) and the American Academy of Neurology (AAN) were reviewed.

Sympazan is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome in patients 2 years of age or older. It may cause an increased CNS depressant effect when used with alcohol or other CNS depressants. Antiepileptic drugs increase the risk of suicidal ideation and behavior. Symptoms may occur with rapid dose reduction or discontinuation, so gradual discontinuation is recommended. Alcohol increases blood levels of this medication by about 50%. It is a schedule 4 controlled substance and there are boxed warnings. Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and duration to the minimum required. Follow patients for signs and symptoms of respiratory depression and sedation. Dosage recommendations were reviewed. It is available in an oral film formulation. In terms of pregnancy, animal data shows it may cause fetal harm. Mild and moderate hepatic impairment requires a dose reduction recommendation. There is no information on severe hepatic impairment.

Oxtellar XR received an expanded indication by the FDA in December 2018 to include monotherapy to treat partial onset seizures in patients 6 years of age and older. Previously, it was only approved as adjunctive therapy in this age group. It is indicated for the treatment of partial-onset seizures in patients 6 years of age and older. Dosage recommendations were reviewed. It is available in an extended-release tablet formulation.

Lyrica received an expanded indication by the FDA in May 2019 to include adjunctive therapy in the treatment of partial-onset seizures to include patients 1 month old to less than 4 years of age. Dosage recommendations were reviewed. It is available in capsule and oral solution formulations.

Nayzilam was approved by the FDA in June 2019. It is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age or older. It may cause an increased CNS depressant effect when used with alcohol or other CNS depressants. Antiepileptic drugs increase the risk of suicidal ideation and behavior. It is associated with a high incidence of partial or complete impairment of recall for the next several hours. Dosage recommendations were reviewed. It is available as a single-dose nasal spray.

In July 2019, Dilantin received the addition of a new warning regarding angioedema, which has been reported. Serious dermatologic reactions warning was updated to include severe cutaneous adverse reactions (SCARs), acute generalized exanthematous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS).

The utilization report was reviewed and 95.4% were for preferred products.

There were no industry comments.

Dr. Umang Patel noted that at the last review, a motion for therapeutic alternatives passed unanimously.

DR. CARLSON MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. WHITE. THE MOTION PASSED UNANIMOUSLY.

Central Nervous System: Antipsychotics - Atypical (Red Class)

Dr. Umang Patel gave the Magellan presentation on Central Nervous System: Antipsychotics - Atypical. Schizophrenia is the most common psychotic illness and affects 1% of the population. Between 25% and 50% of schizophrenic patients attempt suicide with 10% succeeding. Symptoms include delusions, hallucinations, disorganized speech, disorganized or catatonic behavior, and negative symptoms including delusions, hallucinations, or disorganized speech. The guidelines from the American Academy of Child and Adolescent Psychiatry (AACAP) were reviewed.

Bipolar disorder has a lifelong prevalence and ranges from 0.9% to 2.1% of the population. It is characterized by episodes of mania, depression, or a mixed state. Criterion used to diagnose bipolar I disorder is the presence of a manic episode (persistent elevated, expansive, or irritable mood for at least one week with increased energy and activity) or a mixed features specifier (rapidly alternating polarity of mood, sadness, irritability, and mania for at least one week), and three or more other characteristic symptoms. These symptoms include inflated self-esteem or grandiosity, decreased need for sleep, more talkative than usual or pressured speech, flight of ideas or feelings of racing thoughts, distractibility, increase in goal-directed activity or psychomotor agitation, and excessive involvement in risky, pleasurable activities. Guidelines from the American Psychiatric Association (APA) were reviewed.

Tourette's disorder has an unknown prevalence, but observational studied have suggested the prevalence of 1% in school-aged children. It is a genetic disorder characterized by motor and vocal tics. Generally, individuals have repetitive, stereotyped movements of vocalization (sniffing, muscle tension, blinking). DSM-5 criteria for Tourette's disorder states multiple motor and at least one vocal tic present during the illness (not necessarily simultaneously) and have been present for at least one year or longer, although they may wax and wane in frequency. Onset of these symptoms must occur prior to 18 years of age to be considered Tourette's disorder. Peak tic severity typically occurs between the ages of 10 and 12 years. Tics usually improve during adolescence, with 18% of those older than 16 years of age experiencing no tics and 60% having minimal or mild tics for six years after initial examination. The guidelines from the American Academy of Neurology were reviewed.

The FDA expanded the indication for Vraylar to include the treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults. It is contraindicated with MAOIs. There is a black boxed warning for increased risk of suicidal thinking and behavior. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Vraylar is not approved for the treatment of patients with dementia-related psychosis. Dosage recommendations were reviewed. It is available in capsule formulation.

Teva will discontinue Orap in both strengths of its tablet formulation based on a business decision. Generics are available.

The utilization report was reviewed and 92% of prescriptions were for preferred products.

PAUL THOMPSON, a representative of Alkermes, discussed Aristada Initio, which was approved by the FDA in June 2018. Aristada and Aristada Initio are both aripiprazole lauroxil crystals. Aristada is an extended-release, injectable, long-acting antipsychotic indicated for the treatment of schizophrenia. Aristada Initio, in combination with oral aripiprazole, is indicated for the initiation of Aristada when treating schizophrenia in adults. The main difference is the particle sizes of the two molecules. Aristada Initio has smaller particle size and releases quicker, which allows for a one-day initiation regiment for long-acting Aristada. There is a black boxed warning of increased mortality in the elderly. There are two options of initiating Aristada, 21 days of oral aripiprazole or the Aristada Initio initiation regimen. Aristada Initio is only available in 675 milligrams. There is a risk of dosing errors, compared to the long-acting version of Aristada. It should not be used in patients with CYP2D6 poor metabolism or inhibitors or inducers of 2D6 and 3A4. It can be administered in the deltoid muscle. Prescribers should assess for tolerability before starting long-acting Aristada. Side effects include headache, insomnia and injection site reactions. Several studies and their outcomes were reviewed.

VALERIE NG, a representative of Indivior, discussed Perseris. Perseris is indicated for the treatment of schizophrenia in adults. What makes it different is that it is the first and only once-monthly extended-release formulation of risperidone. It is also the first and only second-generation atypical antipsychotic that is injected subcutaneously. Neither a loading dose nor a supplemental oral dose is recommended for Perseris because it only takes four to six hours to reach near steady state when using Perseris. It was formally launched in the marketplace in February of 2019 and met all the statistically significant measures on the positive/negative syndrome scale score and the clinical global impression severity of skill scores. Perseris is not currently on the updated PDL. We respectfully request that Perseris be added to the PDL so that patients suffering from schizophrenia can have another option.

Dr. Semling noted that Perseris was on the PDL, but it was a non-preferred agent. Prescribers can use the medically necessary clause to prescribe Perseris, as long as it is not on the suspend list, which requires prior authorization.

In response to Dr. Phillips, Ms. Ng said Perseris comes in 90 milligrams, which corresponds to 3 milligrams of oral risperidone; and 120 milligrams, which corresponds to 4 milligrams of oral risperidone. The label states that if you are stable on oral medication, Perseris is not recommended. However, someone who is unstable on 6 milligrams of risperidone may not be adherent to their oral medication and Perseris could be an alternative for them since it is a once-a-month formulation. We are also in the process of formulating a product that would meet the demands of patients on higher doses of risperidone. It is subcutaneously injected into the abdominal area, but we are look into an alternative injection site such as under the arm.

Erin Narus noted that while patients using 6 milligrams of risperidone may not be responding due to adherence, there is also the possibility that they are not responding to the medication for other reasons.

In response to Erin Narus, Ms. Ng reviewed the risks associated with Perseris. Risperidone is very similar to the systemic safety profile of oral risperidone. The main difference is injection site reactions. Adverse effects include headache, nausea, muscular skeletal pain, and weight gain.

Dr. Ruggles noted that the medically necessary clause did not have criteria that had to be met. The provider states on the prescription that the drug is medically necessary and provides justification for why he wants it prescribed.

MAE KWONG, a representative of Jansen, thanked the committee for making Invega Sustenna and Invega Trinza available on the PDL. Both are long-acting injectable atypical antipsychotics containing paliperidone palmitate. Invega Sustenna is a once-monthly injection. Invega Trinza is the only long-acting injectable delivered every three months after a patient has been on Sustenna for at least four months. Several studies and their outcomes were reviewed. Multiple studies have demonstrated improvement in adherence, persistence, and health care outcomes for Sustenna. These positive outcomes lower medical costs, which offsets pharmacy costs associated with long-acting injectables. The burden of schizophrenia remains substantial in the U.S. Oral antipsychotic adherence rates are low and relapse is common and costly. Clinical guidelines recommend long acting injectables. The long-term economic impact of patients on Sustenna has shown reduction in reincarceration, health care utilization, and cost. Patients who are perfectly transitioned to Invega Trinza's 3-month injectable from Sustenna demonstrate high adherence, high persistent and economic benefits or neutrality to Sustenna. We request that Invega Sustenna and Trinza be maintained as an option for schizophrenia patients in Alaska and consider the benefits of long-acting injectables over oral antipsychotics.

In response to Erin Narus, Ms. Kwong said the adverse events with Invega included injection site reactions, sedation, somnolence, dizziness, extra paramita thyroid disorders, and weight gain.

AITEN PATADIA, a representative of Otsuka, said he had no formal testimony prepared, but was happy to answer questions about their products.

In response to Dr. Phillips, Mr. Patadia said Abilify Mycite was an aripiprazole tablet with an ingestible marker inside the medication. A patch is attached to the patient's arm and monitors whether

the medication had been taken. The patch is attached to the arm by adhesion and is worn for seven days. If a patient decided to remove the patch, it could be removed. Four patches are provided in each system.

Dr. Phillips noted that she had read that this was a combined effort between Otsuka and Magellan Health. Dr. Umang Patel said Magellan has a separate arm of the company that works in behavioral health, but it is not intertwined with the arm of the company that does that presentations before the committee. Dr. Phillips felt this information should have been disclosed to the committee. Dr. Carlson said it was a very important transparency issue that had not been mentioned. Erin Narus said staff would discuss the issue with Magellan and report back to the committee.

Dr. Ruggles noted that at the last review, a motion for therapeutic alternatives, to include at least one oral preparation; one intramuscular injection; and two long-acting intramuscular injectables, one of which has a duration of at least four weeks, passed unanimously.

Dr. Phillips expressed some concerns about Relprevv's FROG use. Nuplazid may be important for certain populations, but it has no indication for schizophrenia or bipolar disorder.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, TO INCLUDE AT LEAST ONE ORAL PREPARATION; ONE INTRAMUSCULAR INJECTION; AND TWO LONG-ACTING INTRAMUSCULAR INJECTABLES, ONE OF WHICH HAS A DURATION OF AT LEAST FOUR WEEKS. SECONDED BY DR. DORAN-ATCHISON. THE MOTION PASSED UNANIMOUSLY.

Central Nervous System: Antidepressants (Red Class)

Dr. Umang Patel gave the Magellan presentation on Central Nervous System: Antidepressants. Prevalence of 12-month and lifetime major depressive disorder (MDD) is approximately 17.3 million American adults or 7.3% of the U.S. population. Women experience depression more often than men. The prevalence of depression in 2017 was estimated at 3.2 million adolescents age 12 to 17. With appropriate treatment, 70% to 80% of patients experiencing MDD achieve a response. However, as many as one-half of all patients do not experience sufficient symptom improvement with initial treatment. Among patients who remit, residual symptoms are common and associated with impaired psychosocial functioning and increased relapse rates. Until recently, known differences among antidepressant drugs were generally limited to safety and tolerability issues. However, over the past few years, a number of studies have emerged to evaluate possible differences among antidepressant classes and their ability to resolve specific symptoms of depression. Each of the groups of drugs in this class has a potential role in the treatment, primarily as a result of their heterogeneous spectrums of activity. As with many psychotropic drugs, patients failing to respond to one type of antidepressant may respond to a switch to, or augmentation with, an antidepressant with another mechanism of action.

Generalized anxiety disorder (GAD) affects 2.7% of the adults U.S. population annually, and women are 60% more likely to be affected by anxiety in their lifetime. The disorder develops gradually and can begin across the life cycle, though the risk is highest between childhood and middle age. It is diagnosed when a person worries excessively about a variety of everyday problems for at least six months or patients are unable to get rid of their concerns, even though they usually realize that their anxiety is more intense than the situation. Physical symptoms that often accompany the anxiety include

fatigue, headaches, muscle tension, muscle aches, difficulty swallowing, trembling, twitching, irritability, sweating, nausea, and hot flashes.

Social anxiety disorder (SAD) is the most common anxiety disorder in the U.S., affecting approximately 5.3 million people per year. It is the third most common psychiatric disorder after depression and alcohol abuse. It is characterized by a marked and persistent fear of social or performance situations in which embarrassment may occur. Women and men are equally likely to develop the disorder, which usually begins in childhood or early adolescence. Social anxiety disorder is often accompanied by other anxiety disorders or depression, and substance abuse may develop if people try to self-medicate their anxiety.

Panic disorder is a severe, chronic anxiety disorder characterized by recurrent episodes of panic and the development of fear or anxiety regarding the possibility of future panic attacks. It occurs in three to six million people per year with one-half to two-thirds of those affected being female. Up to 15% of the general population experience isolated panic attacks, whereas up to 3.5% develop full panic disorder during their lifetime.

Vasomotor symptoms (VMS) associated with menopause, such as hot flashes and night sweats, often are considered the most bothersome symptoms of menopause and affect approximately 75% of women over the age of 50 years. The Endocrine Society recommends SSRIs, SNRIs, gabapentin, or pregabalin for moderate to severe VMS in patients with contraindications to hormone therapy or who choose not to use hormone therapy. Paroxetine mesylate is the only SSRI approved to treat VMS. The American Association of Clinical Endocrinologists (AACE) state that therapeutic trials of nonhormonal medications, such as clonidine, SSRIs or gabapentin, may be considered for the relief of menopausal symptoms in women with no contraindications. The American College of Obstetricians and Gynecologists (ACOG) state SSRIs, SNRIs, clonidine, and gabapentin are effective alternatives to hormone therapy for the treatment of VKS related to menopause.

The guidelines of the American Psychiatric Association (APA), the American College of Physicians (ACP), the National Institution of Mental Health (NIMH), the American Academy of Pediatrics (AAP), and the North American Menopause Society and National Network on Depression Centers were reviewed.

Spravato was approved by the FDA in March 2019 for the treatment of treatment-resistant depression (TRD) in adults. It is a schedule 3 controlled substance. There is a boxed warning for risk of dissociation and sedation after administration as well as abuse and misuse. Patients should be monitored for two hours following administration to mitigate these risks. Due to the potential for abuse and misuse, practitioners should consider the risks and benefits of prescribing and monitor for signs and symptoms. Dosage recommendations were reviewed. It is available as a nasal spray formulation as well as a kit. It may cause fetal harm in pregnant patients and so pregnancy, planning, and prevention is advised. No dose adjustments are needed in patients with mild to moderate hepatic impairment, although patients with moderate impairment may need additional monitoring for adverse reactions.

Zulresso is indicated for the treatment of postpartum depression in adults. It must be administered in the presence of a health care provider in order to provide continuous monitoring during the infusion. It is a schedule 4 controlled substance. It has a REMS program to address the risk of serious harm resulting from excessive sedation and sudden loss of consciousness. Like all antidepressants, Zulresso

carries a warning for suicidal thoughts and behaviors. Dosage recommendations were reviewed. It is available in a single-dose vial for continuous intravenous infusion.

Drizalma Sprinkle is indicated for major depressive disorder in adults, generalized anxiety disorder in adults and pediatric patients 7 to 17 years of age, diabetic peripheral neuropathic pain in adults, and chronic musculoskeletal pain in adults. It is contraindicated with MAOIs as it can cause serotonin syndrome. It carries a black boxed warning of increased risk of suicidal thinking and behavior. Dosage recommendations were reviewed. It is available in a delayed-release capsule formulation.

The utilization report was reviewed. Last year it was stratified by SSRIs and others. For SSRIs, 97.4% of the prescriptions were for preferred products. For antidepressants, 92.3% of the prescriptions were for preferred products.

MAY KWONG, a representative of Jansen, discussed Spravato, which was given a breakthrough designation status by the FDA. On March 5, 2019, Spravato maintenance spray was approved, which is an NMBA antagonist and is the first new mechanism of action for antidepressants in over a decade. It is used in conjunction with an oral antidepressant for adults who have failed to respond to at least two different antidepressants of adequate dose and duration. Spravato is a schedule 3 controlled substance and is only available with a REMS program. It is patient administered under the direct observation of a health care provider and patients are required to be monitored afterwards. It will never be dispensed directly to a patient for home use. Dosing recommendations were reviewed. Several studies and their outcomes were reviewed. The most common adverse events were disassociation, dizziness, nausea, and vertigo. Blood pressure increases were observed in 10% of patients. Discontinuation rates were less than 5%. We respectfully request the committee include Spravato nasal spray on the Alaska PDL.

In response to Dr. Phillips, Ms. Kwong said the clinical trial patient population had to fail two antidepressants, which included both SSRIs and SNRIs, before being enrolled in the study. The treatment resistant studies were limited to four oral antidepressants. The PI had an option of choosing one of the four oral antidepressants as long as it had not previously been prescribed to the patient.

In response to Dr. Doran-Atchison, Ms. Kwong reviewed the REMS program. Spravato, although patient administered, is not dispensed directly to the patient. It is typically administered in a doctor's office, clinic, or treatment center.

Dr. Ruggles read last year's motions. A motion that antidepressants, SSRIs, were therapeutic alternatives passed unanimously. A motion that antidepressants, others, were therapeutic alternatives passed unanimously.

Dr. Ruggles felt that antidepressants, SSRIs, should have been class effect instead of therapeutic alternatives because it is all the same mechanism of action.

Dr. Phillips agreed that the SSRIs should be a class effect. She noted that only two antidepressants were approved for children were Prozac and Lexapro and should be included in PDL.

DR. PHILLIPS MOVED THE ANTIDEPRESSANTS, SSRIs, WERE CLASS EFFECT.

In response to Dr. Carlson, Erin Narus said grandfathering would be taken into consideration if there were any changes to the PDL. It could also be included in the motion.

DR. CARLSON MOVED A FRIENDLY AMENDMENT TO THE MOTION TO GRANDFATHER SUCCESSFULLY MANAGED PATIENTS. THE MAKER OF THE MOTION ACCEPTED THE FRIENDLY AMENDMENT.

THE AMENDED MOTION WAS SECONDED BY DR. CARLSON. THE MOTION PASSED UNANIMOUSLY.

Dr. Ruggles asked for further comments on Antidepressants, Others.

Dr. Phillips said patient were looking forward to Spravato, but she was concerned that the expectations were more than could be delivered. The studies were limited, especially for the long-term effects.

Dr. Semling explained that billing for Spravato was limited to medical benefits, rather than pharmacy benefits, to ensure that it would be administered in a proper location.

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

Break from 10:35 a.m. to 10:46 a.m.

Erin Narus spoke about the concern expressed earlier in the meeting regarding Magellan's relationships to industry. Magellan will be asked to provide a list of disclosures for all industry relationships that they have under any of their arms and to explain the nature of those relationships. These disclosures will be provided to the committee four weeks before each meeting, and Magellan will update those disclosures before each subsequent meeting to ensure transparency.

On the abilifymysite.com initial rollout, the website reads as follows. In August 2018, Otsuka announced it had signed a collaborative agreement to facilitate access to the ABILIFY MYCITE System to select regional provider networks contracted through Magellan Health. Further, in June 2019, Otsuka announced that the ABILIFY MYCITE System is available to patients via the Thriving Mind South Florida network. These agreements create the opportunity for physicians and adult patients to gather experience in real-world settings with the system.

Staff wants to ensure that testimony is transparent, balanced, and in compliance with all federal regulations and statutes. There have been times where the information provided fell outside of the regulations for drug promotion and labeling. Industry should be aware of their responsibility to ensure they follow drug promotion and labeling guidelines. Labeling also includes anything spoken by pharmaceutical manufacturers, so all comments should be fair and balanced. We recommend that manufacturers speak only to their specific studies. A good reference for the promotion and labeling requirements is under federal regulations 21 CFR 201 and 202. Additional information on our position will be posted to our website for manufacturers.

If staff overlooks any of these issues, please provide us with a written letter to outline anything that appears to be unbalanced or concerns with testimony or information provided. The Office of Prescription Drug Promotion has guidance on how to report issues of concern.

Central Nervous System: Alzheimer's Agents (Green Class)

Dr. Umang Patel gave the Magellan presentation on Central Nervous System: Alzheimer's Agents. The utilization report was reviewed and 84% of the prescriptions were for preferred products. At the last review, a motion for therapeutic alternatives passed unanimously.

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

4-C. Analgesics: NSAIDs (Blue Class); Analgesics, Opioid - Short Acting (Red Class); Analgesics, Opioid - Long-Acting (Blue Class); Neuropathic Pain (Blue Class); Antimigraine Agents (Red Class); Skeletal Muscle Relaxants (Green Class); Restless Leg Syndrome (RLS) (Green Class)

Analgesics: NSAIDs (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Analgesics: NSAIDs. NSAIDs are commonly used to treat rheumatoid arthritis, osteoarthritis, and pain from various etiologies. They are the most widely used drugs in the U.S., with approximately 80 million prescriptions being filled yearly, which accounts for roughly 4.5% of all prescriptions. It is estimated that over the counter NSAIDs are used five to seven times more often than prescription NSAIDs. Most oral NSAIDs are now available as generics and are generally considered to be safe and effective. NSAIDS are associated with adverse effects including GI bleeding, peptic ulcer disease, hypertension, edema, and renal disease. NSAIDs have been linked to an increased risk of myocardial infarction which is reflected in the boxed warning for all NSAIDs. In July 2015, the FDA issued a Safety Alert strengthening the warning on an increased risk of heart attack and stroke risk associated with NSAIDs. There are no guidelines updates.

In March of 2019, the FDA expanded the indication for Flector to include patients 6 years of age and older for the topical treatment of acute pain due to minor strains, sprains, and confusions. There is a boxed warning for CV thrombotic and GI events. Dosage recommendation were reviewed. It is available as a topical system formulation.

The utilization report was reviewed and 99% of the prescriptions were for preferred products.

There were no industry comments.

Dr. Ruggles noted that last year's motion of therapeutic alternatives passed unanimously, but class effect might be more appropriate.

DR. PHILLIPS MOVED A CLASS EFFECT. SECONDED BY DR. DORAN-ATCHISON. THE MOTION PASSED UNANIMOUSLY.

Analgesics: Analgesics, Opioid - Short-Acting (Red Class)

Dr. Umang Patel gave the Magellan presentation on Analgesics: Opioid - Short-Acting. While definitions vary, chronic pain is generally defined as pain lasting three months or more or past the time required for normal tissue healing. Approximately 11.2% of adults report daily pain, which is greatly misunderstood. Historically, data suggests that pain may be undertreated, but newer estimates imply that opioid treatment or pain may be over utilized. An estimated 20% of patients presenting to outpatient providers with noncancerous pain or pain-related diagnoses, whether acute or chronic, receive an opioid prescription. Likewise, per capita opioid prescriptions increased by 7.3% from 2007 to 2012, with prescribers writing 66.5 opioid prescriptions for every 100 Americans in 2016. Approximately 165,000 people have died from overdoses related to opioid pain medications in the U.S. from 1999 to 2014. Drug related deaths have tripled from 1999 to 2015; and during 2015 alone, 33,091 persons in the U.S. died from opioid-related overdoses. Opioid-related overdose was higher among males (13.7%) in comparison to females (7.1%). Despite this, persistent pain that is uncontrolled may have clinical, psychological, and social consequences; thus, it is critical to weigh the risks and benefits of opioid use and reevaluate patients routinely for appropriate dose, duration, and treatment choice, including both pharmacologic and nonpharmacological modalities.

The guidelines from the American College of Obstetricians and Gynecologists (ACOG), the Department of Health and Human Services (DHHS), the World Health Organization (WHO), the National Comprehensive Cancer Network (NCCN), the FDA, the CDC, HIV Medicine Association (HIVMA) of the Infectious Disease Society of America (IDSA), and the American Association of Oral and Maxillofacial Surgeons (AAOMS) were reviewed.

Dsuvia is indicated for use in adults in a certified medically supervised health care setting, such as hospitals, surgical centers, and emergency departments for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Warnings include serious, life-threatening, or fatal respiratory depression, so close monitoring is required. Dsuvia exposes users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Accidental exposure to or ingestion, especially in children, can result in respiratory depression and death. It is a schedule 2 controlled substance that should only be administered by a health care provider. Dosage recommendations were reviewed. It is available in a sublingual tablet formulation.

Apadaz is a benzhydrocodone/acetaminophen combination. It is indicated for short-term management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, Apadaz should be reserved for patients for whom alternative treatment options such as nonopioid analgesics have not been tolerated or have not provided adequate analgesia. Dosage recommendations were reviewed. It is available in immediate-release tablet formulation.

The utilization report was reviewed and 48.5% of the prescriptions were for preferred products.

Dr. Semling referenced the utilization report. Hydrocodone/acetaminophen tablets were all lumped together. Tylenol 300 milligram is non-preferred, but Tylenol 325 milligram is preferred, so the actual PDL utilization would be closer to 88% to 90% of prescriptions for preferred products.

There were no industry comments.

Dr. Ruggles noted that at the last review, a motion for therapeutic alternatives passed unanimously.

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

Analgesics: Analgesics, Opioid - Long-Acting (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Analgesics: Opioid - Long-Acting. The background was discussed in the opioid - short-acting class. The guidelines from the Department of Health and Human Services (DHHS) were reviewed. Buprenorphine received a new generic approval of ANDA from Teva/Actavis Pharmaceuticals. An authorized generic version is available from Rhodes Pharmaceuticals.

The utilization report was reviewed and 64.7% of prescriptions were for preferred products.

There were no industry comments.

Dr. Ruggles said at the last review, a motion for therapeutic alternatives to include at least one oral preparation, one transdermal preparation, and at least one abuse-deterrent preparation passed unanimously.

DR. RYAN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE ORAL PREPARATION, ONE TRANSDERMAL PREPARATION, AND AT LEAST ONE ABUSE-DETERRENT PREPARATION. SECONDED BY DR. PHILLIPS.

The committee discussed why the utilization report was so low. Dr. Ruggles noted that there had been a shortage of OxyContin generic drugs, so the brand-name drug was utilized.

THE MOTION PASSED UNANIMOUSLY.

Analgesics: Neuropathic Pain (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Analgesics: Neuropathic Pain. It has recently been defined as the pain that evolves as a result of direct injury or disease to the nervous system, specifically the somatosensory system. Neuropathic pain can be caused by a number of different diseases such as diabetes mellitus, herpes zoster, human immunodeficiency virus, and medical interventions.

Guidelines from the Mayo Clinic, the American Academy of Neurology (AAN) for Management of Diabetic Neuropathic Pain, and the American Academy of Neurology (AAN) for Treatment of Post herpetic Neuralgia.

Drizalma Sprinkle was reviewed in the antidepressants class, but it has a dual indication. Its new indication is for diabetic peripheral neuropathic pain in adults. Limitations include contraindications with MAOIs. There is a black boxed warning of increased risk of suicidal thinking and behavior. Dosage recommendations were reviewed. It is available as delayed-release sprinkles.

The utilization report was reviewed and 96.3% of prescriptions were for preferred products.

There were no industry comments.

Dr. Ruggles said at the last review, a motion of therapeutic alternatives passed unanimously.

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

Analgesics: Antimigraine Agents (Red Class)

Dr. Umang Patel gave the Magellan presentation on Analgesics: Antimigraine Agents. Migraine accounts for 10% to 20% of all headaches in adults and affects over 39 million men, women, and children in the U.S. Headache is one of the most common complaints by patients when presenting to a physician. About 64% of physician-diagnosed patients who experience migraines and 41% of undiagnosed migraine sufferers reported severe impairment or the need for bed rest due to their migraine symptoms. In addition, 18% of women, 6% of men, and 10% of children experience migraine, an epidemiologic profile that has remained stable over many years. Approximately 85% of patients with migraine headaches suffer less than three to four attacks per month. Migraine headaches must be differentiated from tension-type headaches. Key criteria for the diagnosis of migraine headaches include an episodic headache lasting from 4 to 72 hours with at least two of the following symptoms: unilateral pain, throbbing, aggravated by routine physical activity, and pain of moderate to severe intensity. During the headache, at least one of the following are present: nausea and/or vomiting, or photophobia and phonophobia.

A cluster headache (CH) is a severe, primary headache disorder characterized by extreme pain on one side of the head and autonomic symptoms such as nasal congestion or lacrimation. Headache periods can persist for weeks to months with daily or more frequent attacks of 15 to 180 minutes in duration. The estimated lifetime prevalence more than one in 1,000. These headaches can be either episodic or chronic in nature with episodic being the predominant form. Individuals with episodic CH experience period of attack followed by periods of remission, whereas individuals with chronic CH have minimal to no periods of remission between headache attacks.

The guidelines from the American Headache Society (AHS) and the American Academy of Neurology (AAN) and American Headache Society (AHS) were reviewed.

Ajovy was approved by the FDA in September 2018. It is indicated for preventative treatment of migraines in adults. There is no adequate data in pregnant, pediatric, or geriatric patients. Dosage recommendations were reviewed. It is available in single-dose prefilled syringes.

In March 2019, the FDA approved a new formulation for Aimovig of 140 milligram per milliliter formulation. This medication is also indicated for preventative treatment of migraines in adults. Dosing recommendations were reviewed.

In June 2019, the FDA approved a new formulation and indication for Emgality. The new indication is the treatment of episodic cluster headaches in adults. Dosage recommendations were reviewed. It is available as single-dose prefilled syringes. The new availability was 100 milligrams per one milliliter single-dose prefilled syringe.

In January 2019, the FDA approved Tosymra for acute treatment of migraine with or without aura in adults. It should be used only if a clear diagnosis of migraine has been established. It is not indicated for the preventive treatment of migraine or for the treatment of cluster headaches. It is contraindicated in patients with ischemic or vasospastic CAD. Dosage recommendations were reviewed. It is available in a nasal spray formulation.

The utilization report was reviewed. It is stratified by triptans and others. The utilization for antimigraine agents, triptans was 94.5% of the prescriptions were for preferred products. For the antimigraine agents, others, which had very few units dispensed, was 0% of the prescriptions were for preferred products.

MARIA AGAPOVA, (telephonic), a representative of Teva, discussed Ajovy. Ajovy addresses the limitations that it is a (indiscernible) which may influence adherence. In addition, Ajovy Clinical Program generated a vast body of evidence characterizing the experience of a migraine patient before and after initiating preventive therapy and demonstrating Ajovy is safe and efficacious across migraine populations with the highest unmet needs. Ajovy demonstrated efficacy across multiple dimensions of migraine, not only just frequency of migraines, but intensity and duration. Several trials and their outcomes were reviewed. Multiple options exist for dosing and administration to help patients choose a sustainable regiment. It has rapid onset of effect, as well as long-acting action that enable that quality dosing. It has a positive impact on function, quality of life, and productivity. It is safe and efficacious in patients who have had inadequate response to two, three and four passes of preventative therapies. Several studies and their outcomes were reviewed. We request that Ajovy be available on the PDL.

In response to Dr. Carlson, Ms. Agapova discussed several trials and their outcomes.

Dr. Ruggles said at the last review for antimigraine agents, triptans, a motion of therapeutic alternatives passed unanimously.

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

Dr. Ruggles noted that at the last review for antimigraine agents, others, a motion for therapeutic alternative to both treatment and prevention of migraines passed unanimously.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE BOTH TREATMENT AND PREVENTION OF MIGRAINES. SECONDED BY DR. RILEY. THE MOTION PASSED UNANIMOUSLY.

Analgesics: Skeletal Muscle Relaxants (Green Class)

Dr. Umang Patel gave the Magellan presentation on Analgesics: Skeletal Muscle Relaxants. The utilization report was reviewed and 98.3% of prescriptions were for preferred products. At the last review, a motion of therapeutic alternatives passed unanimously.

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

Analgesics: Restless Leg Syndrome (RLS) (Green Class)

Dr. Umang Patel gave the Magellan presentation on Analgesics: Restless Leg Syndrome (RLS). The utilization report was reviewed and 100% of prescriptions were for preferred products. At the last review, a motion for class effect passed unanimously.

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

4-D. Substance Dependence: Smoking Cessation Products (Blue Class); Opioid Dependence (Blue Class); Opioid Reversal Agents (Green Class)

Substance Dependence: Smoking Cessation Products (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Substance Dependence: Smoking Cessation Products. Updated guidelines from the American College of Cardiology (ACC) were reviewed. The utilization report was reviewed and 97.3% of the prescriptions were for preferred products. At the last review, a motion for therapeutic alternatives to include Chantix passed unanimously.

There were no industry comments.

The committee discussed why Chantix had been included in previous motions. Dr. Ruggles thought it was because Chantix worked better than nicotine. Erin Narus noted that Chantix was currently a preferred product. Dr. Umang Patel said the 2017 minutes reflect that Chantix had accounted for roughly 86% of the prescriptions dispensed, so the committee decided to include it on the PDL. Dr. Ruggles noted that was no longer the case.

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

Substance Dependence: Opioid Dependence (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Substance Dependence: Opioid Dependence. It is estimated that 28.6 million Americans, ages 12 years and older, are currently illicit drug users. There were approximately 11.8 million people, ages 12 and older, in the U.S. who misused opioids between 2016 and 2017. Approximately 20.1 million people, ages 12 and older, were considered to have a substance use disorder in 2016, including 15.1 million with an alcohol use disorder, 7.4 million with an illicit drug use disorder, and 2.1 million with an opioid use disorder. According to the Drug Addiction Treatment Act of 2000, in order to become a qualified practitioner, physicians must be licensed under

state law to practice medicine, obtain a waiver from the U.S. Substance Abuse and Mental Health Service Administration, and notify the Secretary of Health and Human Services of their intention of prescribing or dispensing buprenorphine. Such practitioners hold a modified DEA registration in which they are designated by a unique identifier and must include it on each prescription written. Prescribers are limited in the number of patients they may treat under a waiver, but they may request approval to treat additional patients.

Guidelines from the U.S. Department of Health and Human Services (DHHS) and the U.S. Food and Drug Administration (FDA) were reviewed.

The utilization report was reviewed and 53.6% of the prescriptions were for preferred products.

VALERIE NG, a representative of Indivior, thanked the committee for giving patients access to Sublocade, which is an extended release formulation of buprenorphine, to fight against opiate use disorders.

Dr. Ruggles noted that at the last review, the motion, after a friendly amendment was accepted, was made for therapeutic alternatives to include at least one long-acting injectable product. The motion passed unanimously.

Dr. Semling noted that most of the prescriptions for non-preferred products were brand versus generic formulations.

DR. RILEY MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE LONG-ACTING INJECTABLE PRODUCT. SECONDED BY PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

Substance Dependence: Opioid Reversal Agents (Green Class)

Dr. Umang Patel gave the Magellan presentation on Substance Dependence: Opioid Reversal Agents. The utilization report was reviewed and 100% of the prescriptions were for preferred products. At the last review, a motion for therapeutic alternatives to include Narcan passed unanimously.

DR. GREEAR MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE NARCAN. SECONDED BY DR. CARLSON. THE MOTION PASSED UNANIMOUSLY.

4-E. Antiviral Monoclonal Antibodies: Respiratory Syncytial Virus (Green Class)

Antiviral Monoclonal Antibodies: Respiratory Syncytial Virus.

Dr. Umang Patel gave the Magellan presentation on Antiviral Monoclonal Antibodies: Respiratory Syncytial Virus. The utilization report was reviewed and 100% of the prescriptions were for preferred products. At the last review, a motion to add Synagis to the formulary as a class effect passed unanimously.

DR. PHILLIPS MOVED TO ADD SYNAGIS TO THE FORMULARY AS A CLASS EFFECT. SECONDED BY DR. GREEAR. THE MOTION PASSED UNANIMOUSLY.

Dr. Ruggles thanked everyone for their participation in the meeting and noted that the next meeting would be January 17, 2020. The committee moved into a closed session.

5. Review Minutes from September 2019.

6. Comments from Committee Members or Chair

7. Adjourn

DR. PHILLIPS MOVED TO ADJOURN THE MEETING. SECONDED BY DR. GREEAR. THE MOTION PASSED UNANIMOUSLY.

The meeting adjourned at 11:52 a.m.