Alaska Medicaid Pharmacy and Therapeutics Meeting

MINUTES OF MEETING
November 18, 2022

Committee Members Present:
John Riley, PA, Acting Chairman
Robert Carlson, MD
Diane Liljegren, R.Ph.
Matthew Bagay Bruno,
Sarah Doran-Atchison, PharmD
Claudia Phillips, MD
Charles Ryan, MD
Trish White, R.Ph.

Committee Members Absent:
Jonathan Harrison, PharmD

Others Present:
Ryan Ruggles, Pharm D
Charles Semling PharmD
Kristie Kapinas, Vertex
Lynda Finch, BioGen
Shirley Kwatch, Novartis
Debbie Sheppe, Neurelis
Kenneth Berry, Alkermes
Julia Overman, Corium
Tammy Martin, Biohaven
Charlie Lovan, AbbVie
Rochelle Yang, Teva

1. Call to Order – Chair

Mr. Riley called the meeting to order.

2. Roll Call

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

3. Public Comments - Local Public/Health Practitioners

None.

4. Class Review, Discussion & Vote

4-A. Cystic Fibrosis: CFTR potentiator class (Red); Inhaled Antibiotics (Green); Pancreatic Enzymes (Green)

Cystic Fibrosis: CFTR potentiator class (Red Class)

Ryan Ruggles gave the Magellan presentation for Cystic Fibrosis: CFTR potentiator class. Cystic fibrosis is a serious autosomal recessive multi organ disorder. It affects approximately 31,411 children and adults in the US, and is the most common fatal genetic disease in Caucasians. The median survival rate in patients with cystic fibrosis is about 50 years with 80% reaching adulthood. Children are anticipated to live to approximately 40 years of age with current treatments, and in 2020 adults comprised about 57.2% of the CF population, while in 1990, they comprised approximately 32.1%. Mutations lead to the disease of the exocrine gland function resulting in the formation of a thick mucus that builds up in the lungs, digestive tract and other parts of the body. CFTR functions as a chloride channel, and mutations in here lead to abnormalities in the chloride transport along the epithelial cells on mucosal surfaces. The goals of treatment are maintaining lung function by controlling infections or mucus, maintaining appropriate growth by providing nutritional support and managing disease complications.

Treatment guidelines were reviewed.

In December 2020, the FDA approved Kalydeco for the treatment of cystic fibrosis in patients aged four to less than six months of age, and weighing 5 kilograms or more, who have one or more mutations in the CFTR genetics responsive to Ivacaftor based on clinical and/or in-vitro assay data. Previously, this was only approved in patients six months of age or greater. There are no other changes to the dosage or availability. This medication is a Category B as in beta pregnancy class. There is no dose adjustment for patients with mild to moderate renal impairment and there are no studies for severe or end stage renal disease in this medication.

In September 2022, the FDA approved an expanded indication for Orkambi for the treatment of CF in patients greater than or equal to 1 year of age who are homozygous for the F508del mutation and a CFTR gene, previously indicated for patients greater than or equal to 2 years of age.

Public Comments for Cystic Fibrosis: CFTR potentiator class (Red Class)

KRISTIE KAPINAS, a representative of Vertex Pharmaceuticals, provided public testimony on behalf of Vertex CFTR modulators. CFTR modulators are the only medications for CF that work by targeting the underlying cause of CF. There are currently four CFTR modulators approved for the treatment of CF, based on age and genotype. The four modulators are Trikafta, Symdeko, Orkambi and Kalydeco.

In September 2022 the FDA approved the expanded use of these medications to include children ages 12 to less than 24 months who are homozygous for the F505del CFTR mutation.

Orkambi was previously approved by the FDA for use in people with CF ages 2 years and older with 2 copies of the F508del mutation. Orkambi is the only FDA approved CFTR modulator indicated for patients with CF aged 1 year and older who are homozygous for the F508del CFTR mutation. This recent label expansion is supported by results from a phase 3, two-part, open label trial of Orkambi that enrolled children aged 1 to less than 2 years of age, at screening, who were homozygous for the F508del mutation referred to as Trial 7 in the USPI. The full results from this study were published in the American Journal of Respiratory and Critical Care Medicine and demonstrate the safety, tolerability and pharmacodynamics of Orkambi in this young population. A full list of warnings and precautions for each modulator can be found in the prescribing information.

DR. RYAN MOVED THAT THE DRUGS WERE THERAPEUTIC ALTERNATIVES, SECONDED BY DR. LILJEGREN. THE MOTION PASSED UNANIMOUSLY.

Cystic Fibrosis: Inhaled Antibiotics (Green Class)

Ryan Ruggles gave the Magellan presentation for Cystic Fibrosis: Inhaled Antibiotics. There were only 15 claims and 100% non-PDL.

TRISH WHITE MOVED THAT THE DRUGS WERE THERAPEUTIC ALTERNATIVES, SECONDED BY DR. RYAN. THE MOTION PASSED UNANIMOUSLY.

Cystic Fibrosis: Pancreatic Enzymes (Blue Class)

Ryan Ruggles did not give the Magellan presentation for Cystic Fibrosis: Pancreatic Enzymes as he did not have any slide for this.

The utilization report was reviewed and stated that they are roughly 94.4% is in line with the PDL with 187 claims and 11 are non-PDL.

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

Public Comments for Cystic Fibrosis: Pancreatic Enzymes (Blue Class)

CHARLIE LOVAN, a representative from Medical Affairs, spoke about Creon.

Creon is an FDA approved delayed release pancreatic enzyme replacement therapy. It is dedicated for the treatment of exocrine pancreatic insufficiency which will be referred to as EPI for the remainder of this discussion. EPI is a complication of various underlying conditions that lead to insufficient quantity of pancreatic enzymes to a level below normal digestion. EPI results in symptoms such as bloating, flatulence, abdominal pain, fatty stools, diarrhea and unintentional weight loss. The clinical consequences of EPI include that cycle of vitamin deficiencies, malnutrition and impaired quality of life for patients. Creon is available in

3,000, 6,000, 12,000, 24,000 and 36,000 lipase unit strengths. Creon is not interchangeable with any other currently available pancreatic lipase product. Product substitution is not recommended.

There are two studies in adults and children with EPI due to CF and one study in adults with EPI due to chronic pancreatitis. The primary efficacy endpoint was the changing coefficient of fat absorption from baseline to the end of the double-blind period. Statistically significant improvement in the coefficient of that absorption in Creon compared to placebo in all three studies. Adverse reactions occurring in at least two CF patients greater than 4-percent receiving Creon are vomiting, dizziness and cough. Adverse reactions that occurred in at least one chronic pancreatitis patient greater than or equal to 4-percent receiving Creon are hyperglycemia, hypoglycemia, abdominal pain, abnormal feces, flatulence, frequent bowel movements and nasopharyngitis.

It is used to replace the necessary pancreatic enzymes for proper digestion of fats, proteins and carbohydrates needed to maintain adequate nutrition in people with EPI. Unlike other enzymes, Creon has been studied in EPI to the various underlying conditions including CF. Conditions and Creon remains the (unintelligible) of choice by prescribers. AbbVie disrespectfully requests that Creon be maintained as a preferred treatment option for the Alaskan Medicaid patients. Thank you.

4-B. MS Agents: CNS Therapeutic Classes

Public Comments for MS Agents: CNS Therapeutic Classes (Blue Class)

LYNDA FINCH, a representative from BioGen provided some information about Vumerity or diroximel fumarate. Vumerity was approved in October 2019 for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing remitting MS and active secondary progressive MS in adults. Vumerity has a distinct chemical structure from Tecfidera or dimethyl fumarate, but it is converted to the same active metabolite monomethyl fumarate. Because of this bioequivalence we can expect to see the same efficacy and safety as Tecfidera, which has now been prescribed in over 500,000 patients representing 15 million patient years and has long-term data showing efficacy and safety.

With Vumerity, specifically, that was studied for improved patient reported gastrointestinal tolerability versus Tecfidera. There are now over 20,000 patients that have been treated with Vumerity. The specific study was called EVOLVE-MS-2. This was a phase 3 randomized active controlled 5-week head-to-head study to evaluate patient reported GI tolerability for Vumerity versus Tecfidera in relapsing remitting MS patients. Patients that were treated with Vumerity have a statistically improvement in a patient reported outcome measuring GI adverse events symptom intensity. What is important is that the adverse events that lead to study discontinuation, specifically for GI, were 0.8% for Vumerity versus 4.8% in Tecfidera. We have now collected long-term real-world data and that has reinforced that patients are highly adherent to Vumerity with a mean PDC of 91.4%. That is consistent with what we saw in our clinical trial data which has recently been published. Recently the National Institute for Health and Care Excellence, or NICE, published guidance recommending droxicam fumarate or Vumerity as a first line, DMD option for treatment of active relapsing remitting MS. In this disease, it is a

progressive illness and it is really important to have access to the right medication as early in the disease as possible in order to prevent relapse and disability progression. Being able to stay adherent and have a tolerable therapy is an important piece of that. The oral therapies do have very different mechanisms of actions, tolerability profiles and monitoring requirements as well as drug interactions and contraindications. All of those factors are important in selecting the appropriate drug.

To conclude, I would like to ask that you consider adding Vumerity to your preferred drug list as a first line option for patients with relapsing forms of MS. I would like to thank you for your time.

There were no committee questions.

SHIRLEY KWATCH, a representative from Novartis Pharmaceuticals, provided some information about Kesimpta. Kesimpta is FDA approved for the treatment of relapsing forms of RMS to include clinically isolated syndrome, relapsing remitting disease and active secondary progressive disease in adults. Novartis respectfully requests that Kesimpta be added as preferred to the Alaska PDL. Kesimpta slowed disease progression and are the newest, most effective, type of agents used in the MS base and there are currently no B-cell therapy options available on your PDL in a preferred physician. Studies show that DMPs have been most effective when aggressive treatments for highly efficacious therapies have been applied very early in the clinical course of MS delaying disease progression and thus reducing societal economic burden of MS.

Despite multiple disease modifying therapies being available for the treatment of MS, there remains no standard treatment guideline and providers tend to make trade-offs between efficacy and safety when they choose which agent to use. Most recently we have 4 year long term efficacy and safety data for Kesimpta in patients with RMS in the phase 3 ASCLEPIOS I/II trial and ALITHIOS extension study, which was presented and shared at the American Academy of Neurology in April 2022. Kesimpta maintains a similar safety profile as seen in pivotal phase three trials up to 4 years of treatment with no new safety risk identified over the treatment period. Data shows that continuous treatment with Kesimpta for up to 4 years was associated with fewer relapses as well as reduced risk of 3 months and 6 months confirmed disability worsening and less lesion activity versus those who switched. In addition to demonstrating efficacy up to 4 years of continuous treatment with Kesimpta participants who switched from Teriflunomide to Kesimpta in the extension phase demonstrated pronounced reduction in relapses in MRI lesions. The overall rates of adverse events, serious adverse events and overall rates of serious infections were consistent with those observed in the Phase 3 ACLEPIOS I/II trial and did not increase with treatment up to 4 years despite the COVID-19 pandemic.

So, in summary, Kesimpta has the power, precision and flexibility to help MS patients control their disease and offers a highly efficacious self-administered B-cell therapy with a good safety profile. Currently there are no B-cell therapy that is preferred on your PDL. Novartis respectfully requests that Kesimpta be added as a preferred agent. Thank you for your time and consideration.

Ryan Ruggles gave the Magellan presentation on MS Agents: CNS Therapeutic Classes. MS is a complex human autoimmune type inflammatory disease of the CNS. More than 2.3 million people have MS worldwide, 1 million being in the US. It occurs most commonly in Caucasians with rare cases in African Americans and Asian Americans. Although the etiology is predominantly unknown, MS is characterized pathologically by demyelination of 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 complex or complete paralysis. While cognitive impairment occurs in approximately 50% of people with MS, only 10% experienced serious intellectual deterioration. It can be categorized as either relapsing remitting, which is observed in about 85% to 90% of patients or primary progressive. Relapses or attacks typically present sub acutely with symptoms developing over hours to several days, persists for several days to weeks and then gradually dissipating.

The clinical courses fall into one of the following categories with the potential to progress from less severe to more severe. The first being clinical isolated syndrome, which the persons have the first episode of neurologic symptoms due to inflammation or demyelination last at least 24 hours, patients with MRI detected brain lesions consistent with MS are at high risk. Relapsing remitting MS clearly defined self-limited attacks of neurologic dysfunction followed by periods of remission without disease progression. Most patients experienced recovery of function that is often but not always complete.

Primary Progressive MS is where there is nearly continuous worsening of disease, not interrupted by distinct relapses. Some of those individuals have occasional plateaus and temporary minor improvements. Secondary progressive MS is where relapsing remitting disease course at onset, followed by progression with or without occasional relapses, minor remissions and plateaus, and most patients eventually convert to progressive MS.

In December 2021, FDA approved a new formulation of glatiramer, a single sign one phosphate receptor modulator indicated for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing remitting disease and active secondary progressive disease in pediatric patients greater than or equal to 10 years old and weighs greater than or equal to 40 kg. Glatiramer was updated in August 2022. FDA is warning that auto-injector devices that are optional for use with glatiramer acetate injection may not be compatible for use across FDA approved glatiramer acetate injection drug products and has resulted in missed and partial doses. There are currently 3 FDA approved glatiramer acetate injection drug products on the market, all available in a single dose pre-filled syringe with an attached needle for sub-q administration. Patients may administer the dose using only the syringe or by inserting the syringe into an auto-injection. The auto-injectors are reusable and available by prescription separately. The FDA has requested that drug product manufacturers update their labeling to instruct users to confirm the auto-injector is compatible before using it to inject glatiramer acetate.

The utilization showed that roughly 32% was in line with PDL.

DR. RYAN MOVED THAT THE DRUGS WERE THERAPEUTIC ALERNATIVES, SECONDED BY DR. DORAN-ATCHISON. THE MOTION WAS PASSED UNANIMOUSLY.

4-C. ADHD: Stimulants and Related Agents

ADHD: Stimulants and Related Agents (Blue Class)

JULIA OVERMAN, a representative from Corium, provided information about two separate treatments. The first treatment is for ADHD.

First testimony was on Azstarys for ADHD. The first area of focus was to present the unique characteristics. It is a central nervous system stimulant that has been approved for the treatment of ADHD in patients 6 years of age and older, including adults. It is a once daily treatment that is available in 3 dose strengths equivalent to 20, 30 and 40 mg of total dexmethylphenidate. Each capsule contains 2 active ingredients. First, 30% of the capsule is composed of immediate release dexmethylphenidate and 70% is serdexmethylphenidate which is a pro drug of methylphenidate and is the first and only methylphenidate pro drug and is only the second pro drug in the ADHD space. This coformulation of these two molecules is designed to provide both an early onset of action as well as an extended duration. Serdexmethylphenidate, which is the pro drug, is a new molecular entity and is classified as a schedule 4 controlled substance. Azstarys, however, is a schedule 2 controlled substance because it does contain 30% of that immediate release dexmethylphenidate which is a schedule 2 molecule.

She next spoke about the duration of action of Azstarys. It has a unique coformulation that is designed to provide both early onset within 30 minutes and also extended duration of action up to 13 hours. In the clinical trials it demonstrated significant improvement in attention and behavior of children ages 6-12 years of age.

Safety information was also shared. It has demonstrated a safety profile that is consistent to that observed for other methylphenidate products. There is no notable safety signal identified. The most common adverse events during the phase 3 study were upper respiratory tract infection, headache and abdominal pain. There were no adverse events that were considered serious. Refer to the package insert for full information.

Ryan Ruggles 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. ADHD, which has been diagnosed in approximately 15% of children 4 to 17 years of age and 4% of adults, 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, anxiety, as well as aggressive or/and oppositional disorder. And then three main types are primary hyperactive, primary inattentive and mixed.

In 2020, the medical letter suggest that school aged children, adolescents and adults begin with an oral stimulant, noting that none of the agents have been shown to be more effective than another. However, some patients may respond better to amphetamines than to methylphenidate and vice versa. They advise that use of long-acting formulations which generally contain both immediate and extended-release components has become standard clinical practice, and the addition of short acting stimulant may improve symptom control early in the morning or to prolong the duration of action in the afternoon. Alpha-2 agonist, clonidine, guanfacine and the selective norepinephrine reuptake inhibitors, atomoxetine can reduce ADHD symptoms. These agents are considered less effective than stimulants. And the use of pitolisant and solriamfetol were not addressed by the medical letter.

November 2021 the FDA approved a new extended-release tablet formulation of amphetamine for the treatment of ADHD in patients greater than or equal to 6 years of age. The warnings include black box warnings. CNS stimulants have a high potential for abuse and dependance, blood pressure and heart rate increases, moderate blood pressure and pulse. Consider benefits and risks before use in patients who blood pressure increases may be problematic. Psychiatric adverse events; may cause psychotic or manic symptoms in patients with no prior history or exacerbation of symptoms in patients with preexisting psychosis. Evaluate for bipolar disorder prior to use. Pregnancy may cause fetal harm. Dosage recommended to start at 2.5 mg or 5 mg once daily in the morning. Dosage may be increased in increments of 2.5 mg to 10 mg per day every 4-7 days up to a maximum daily dose of 20 mg. Oral suspension can be substituted with tablets on a mg per mg basis. Availability of suspension containing 2.5 mg of phetamine based equivalence per ml and extended-release tablets 5 mg, 10 mg, 15 and 20.

March 2022 the FDA has approved a new transdermal system formulation of dextroamphetamine, Xelstrym. The treatment indication of ADHD in adults and pediatric patients 6 years and older. Similar black box warnings though this also carries the warning of renal impairment. Dose adjustment is recommended for severe renal impairment for ESRV. Pediatric patients 6-17 years recommended starting dose is 4.5 mg per 9 hours. Titrate the dosage in weekly increments of 4.5 mg up to the maximum recommended dose of 18 mg per 9 hours. Recommended starting dose for adults is 9 mg per 9 hours with the maximum recommended dose of 18 mg per 9 hours. Apply 1 transdermal system 2 hours before the effect is needed and remove within 9 hours. Availability if 4.5 mg, 9 mg, 13.5 mg and 18 mg patches.

In April 2022 the FDA approved the expanded indication of viloxazine for use in adults with ADHD. This was previously approved for pediatric patients greater than or equal to 6 years of age. The indication is updated per that change. The dosage for adults is recommended starting at 200 mg once daily titrate in increments of 200 mg weekly up to the maximum recommendation of 600 mg once daily.

In June 2022 the FDA approved methylphenidate ER tablets via 505b2 for the treatment of ADHD in pediatric patients greater than or equal to 6 years of age and adults who are less than or equal to 65 years of age. Treatment of ADHD in adults and pediatric patients 6 years of age is the indication. Black box warning is that CNS stimulants have high potential of abuse and dependance. Blood pressure and heart rate increases. Assess blood pressure and heart rate prior to initiating treatment and following increases in dosage and periodically while on therapy. Long

term suppression of growth. Monitor height and weight at appropriate intervals in pediatric patients. GI obstruction. Avoid use with preexisting GI narrowing. Pediatric patients 6-17 years should have a starting dose of 18 mg once daily. Dosage may be increased by 18 mg once per day at weekly intervals. Maximum dosage for pediatric patients 6-12 years is 54 mg once daily. Max dose for patients 13-17 is 72 mg once daily. Adults starting dose is 18 mg or 36 mg once daily. The dose may be increased by 18 mg once daily at weekly intervals. Maximum dose is 72 mg once daily. Availability is 18 mg, 27 mg, 36, 45, 54, 63 and 72 mg extended-release tablets.

We have the utilization where roughly 98% is in line with the PDL.

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

4-D. Insomnia: Sedative Hypnotics

Insomnia: Sedative Hypnotics (Blue Class)

Ryan Ruggles gave the Magellan presentation on Insomnia: Sedative Hypnotics. In terms of sedative hypnotics, insomnia is a complex symptom that comprises difficulties falling asleep, staying asleep or non-refreshing sleep-in combination with daytime dysfunction or distress. The symptom complex can be independent disorder such as primary insomnia, or the result of another condition which is defined as secondary insomnia. It can be commonly divided into three types based on duration. There's transient insomnia, which lasts up to one week and is often referred to as adjustment sleep disorder because it is caused most often by an acute situational stress such as a test or a deadline. It is often recurrent with the same or similar stresses. The second is short term insomnia, by definition, lasts one to six months and is usually associated with more persistent stressful situations such as death or an illness, or environmental factors such as noise. And lastly, chronic insomnia which is lasting more than six months with a diagnosis established using ICSD-3 or DSM-5 criteria.

In children, the incidence of insomnia in children ranges from 1% to 6%. And 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.

Smith-Magenis syndrome is a genetic disorder of deletion 90% or mutation 10% in chromosome 17, in a section that includes retinoic acid induced one gene. All cases in literature are viewed as spontaneous genetic change, and it affects about 1 in 15,000 to 25,000 individuals in the US. The primary characteristics of this condition include mild to moderate cognitive disability, speech and motor delays, distinctive facial features, skeletal malformations, sleep disturbances and behavioral patterns. Patients may also exhibit reduced sensitivity to pain, visual and hearing abnormalities and a hoarse voice. Other neurologic and organ dysfunction may also be present, and pharmacologic treatments are used to treat various aspects of the disorder. These include medications for sleep disorder including Tasimelteon and melatonin as well as agents for ADHD and seizures.

In January 2022 the FDA approved Quviviq, a rexant receptor antagonist. It is indicated for the treatment of adult patients with insomnia characterized by difficulties with sleep onset and or sleep maintenance. The indication is as stated. CNS depressive effects and daytime impairment. It impairs alertness and motor coordination including morning impairment. Risk increases when used with other CNS depressants. Patients taking Quviviq caution against next day driving and other activities requiring complete mental alertness. Sleep paralysis, hallucinations and cataplexy like symptoms may occur with use. Complex sleep behaviors including sleep walking, sleep driving and engaging in other activities while not fully awake may occur. Discontinue immediately if a complex sleep behavior occurs. Compromised respiratory function. The effect on respiratory function should be considered. Recommended dosage is 25 mg to 50 mg once per night taken orally within 30 minutes of sleep with at least 7 hours remaining prior to planned awakening. It is available in 25 and 50 mg tablets.

There is a discontinuation of Zolpamist in June 2022. It should be available until December 2022 and there are no available generics.

Roughly about 70.9% of prescriptions were in line with the PDL.

DR. LILJEGREN MOVED THE DRUGS WERE THERAPEUTIC ALTERNATIVES, SECONDED BY DR. RYAN. THE MOTION WAS PASSED UNAMIMOUSLY.

4-E. Epilepsy: Anticonvulsants

Epilepsy: Anticonvulsants (Blue Class)

Public Comments on Epilepsy: Anticonvulsants

DEBBIE SHEPPE, a representative from Neurelis, spoke about Valtoco. Valtoco, an intranasal diazepam. She thanked the committee for their recommendation to maintain appropriate access to Valtoco for people with epilepsy in the state of Alaska.

Ryan Ruggles gave the Magellan presentation on Epilepsy: Anticonvulsants. Epilepsy is one of the most common disorders of the CNS. It's defined when a person has two or more seizures. It affects approximately 2.2 million Americans with 150,000 new cases each year. The risk is estimated to be 1% from birth to age 20 years and 3% at age 75.

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 a cluster of cells. Excessive excitability spreads either locally which is partial seizure or widely generalized seizure. Partial seizures begin in one hemisphere of the brain and unless they become secondary generalized, they can cause alterations in motor functioning, sensory symptoms or automatisms. If there is no loss of consciousness, they're called simple partial. If there is loss of or impairment of consciousness, they're called complex partial. About 70% of patients with epilepsy can be maintained on one drug, non-compliance 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.

Just to break down other sub diseases, the disease states in this class, first we have Lennox-Gastaut syndrome. One of the most severe forms of childhood epilepsy and is one of the hardest forms to treat characterized by mental retardation and multiple seizure types, patients have seizures daily, sometimes experiencing several seizures within a day. Patients may also experience drop attacks, which is defined as a loss of muscle control, causing the patient to fall abruptly to the floor. There's infantile spasm, which primarily consists of sudden bending for the body and stiffening of the arms and legs.

West syndrome is characterized by infantile spasms, developmental regression and a specific pattern on the EEG called hypsarrhythmia. The onset is usually in the first year of life, typically between 4 and 8 months and usually stops by age 5, but may be replaced by other seizure types. Lastly, there's Dravet syndrome. It 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 with Dravet Syndrome often experience multiple comorbidities over their lifetime related to the persistent seizure activity, including behavioral and developmental delay. It is associated with 15% to 20% mortality rate, due to sudden unexpected death in epilepsy.

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

In October 2021, FDA approved an expanded indication for oral and IV monotherapy adjunctive therapy in the treatment of partial onset seizures to include patients greater than or equal to 1 month of age to less than 4 years of age, previously indicated for partial onset seizures in patients greater than 4 years of age. Dosage; pediatric patients age 1 month to less than 17 years of age based on body weight and administered orally twice daily.

In November 2021, FDA has approved a new oral solution formulation of topiramate indicated as an initial monotherapy for treatment of partial onset or primary generalized tonic-clonic seizures in patients greater than or equal to 2 years old or as an adjunctive therapy for treatment of partial onset seizures primarily generalized tonic-clonic seizures or seizures associated with Lennox-Gastaut Syndrome and in patients greater than or equal to 2 years of age. It can also be used as a treatment for migraine in patients greater than or equal to 12 years of age. For the Epilepsy indication initial monotherapy for the treatment of partial onset or primary generalized tonic-clonic seizures in patients 2 years of age and older adjunctive therapy for the treatment of partial onset seizures, primary generalized tonic-clonic seizures or seizures associated with Lennox-Gastaut Syndrome in patients 2 years of age and older. Preventative treatment of migraine in patients 12 years of age and older. Warnings of fetal toxicity and use during pregnancy can cause cleft lip and/or palate and being small for gestational age. Suicidal behavior and ideation. Anti-epileptic drugs increase the risk of suicidal behavior or ideation.

Oligohydrosis and hyperthermia. Dosage is stratified by indication. See the package insert provided. It is available in an oral solution of 25 mg/ml.

In March 2022, the FDA has approved a neuroactive steroid gamma aminobutyric acid, a receptor positive modulator, golexanolone, which is indicated for the treatment of seizures associated with psycho independent kinase deficiency disorder in patients greater than or equal to 2 years of age. The indication is as mentioned. Pregnancy warning as this may cause fetal harm. Suicidal behavior and ideation; monitor patients for suicidal behavior and thoughts. Administer orally 3 times daily with food. Dosing for patients' weight 28 kg or less the starting dose is 6 mg three times daily. The maximum dose is 21 mg three times daily. For patients weighing over 28 kg the starting dose is 150 mg three times daily and the maximum dose is 600 mg three times daily. Oral suspension is available in 50 mg/ml.

In April 2022, the FDA has approved fenfluramine for the treatment of seizures associated with Lennox-Gastaut Syndrome in patients who are greater than or equal to 2 years of age. Fenfluramine was already FDA approved for the treatment of seizures associated with Dravet syndrome in patients greater than or equal to 2 years of age. The added to the indication for that drug. The starting dosage for Lennox-Gastaut Syndrome is 0.1 mg per kg twice daily which should be increased weekly based on tolerability. Patients not on (unintelligible) the recommended maintenance dose is 0.35 mg per kg twice daily with the maximum daily dose of 26 mg. The patients taking concomitant stiripentol plus clobazam the recommended maintenance dosage is 0.2 mg per kg twice daily with the maximum dose being 17 mg.

In April 2022, the indication for the treatment of seizures associated with Dravet syndrome in patients taking clobazam has been expanded from patients greater than or equal to 2 years of age to include patients greater than or equal to 6 months of age and weighing at least 7 kg. It is not approved for use as monotherapy. Dosage is 50 mg per kg per day administered by mouth in two or three divided doses depending on the age and weight.

In July 2022, the FDA has approved a new formulation of zonisamide oral suspension indicated as adjunctive therapy for the treatment of partial onset seizures in adults and pediatric patients greater than or equal to 16 years of age. Warnings are serious hematological events such as aplastic anemia and agranulocytosis has been reported with treatment. The availability is 100 mg per 5 ml solution.

In August 2022, the FDA approved midazolam as a 10 mg per 0.7 ml autoinjector for the treatment of status epilepticus in adults approved as a single 10 mg dose given IM in the mid-outer (interposing) using the prefilled injector. Black box warning stating that concomitant use of benzodiazepines and opiates might result in profound sedation, respiratory depression, coma and death. Should monitor patients for respiratory depression and sedation. A second black box warning stating that using this medication exposes users to risks of abuse, misuse and addiction which can lead to overdose or death. Before prescribing this medication, and throughout treatment each patient should be assessed for abuse, misuse and addiction. Final black box warning states that abrupt discontinuation or rapid dose reduction may cause an acute withdrawal reaction which can be life threatening. Neonatal sedation and withdrawal syndrome is possible if

this medication is used during pregnancy. Recommended dose is a single 10 mg dose administered via IM injection using the prefilled auto injector. The availability is as stated above.

When we look at utilization, you can see about 92.1% is in line with a PDL.

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

4-F. Schizophrenia/Bi-Polar Disorder: Antipsychotics

Schizophrenia/Bi-Polar Disorder: Antipsychotics (Blue Class)

Public Comments on Schizophrenia/Bi-Polar Disorder: Antipsychotics

KENNETH BERRY, a representative from Alkermes, spoke about Lybalvi, which is a combination of atypical antipsychotic olanzapine and the opioid antagonist samidorphan. Lybalvi is indicated to the treatment of schizophrenia, or bipolar I, it is contraindicated in patients who are using opioids and who are undergoing acute opioid withdrawal. It has a box warning for increased mortality in elderly patients with dementia related psychosis. In one pivotal study, adult patients were randomized to daily Lybalvi, olanzapine or placebo for four weeks. The primary efficacy endpoint was changed from baseline and PANSS score at week four, and patients treated with Lybalvi showed statistically significant improvement compared to placebo, enhanced total score.

And the second pivotal study, adult patients were randomized to daily Lybalvi or olanzapine for 24 weeks. The co-primary endpoint was percentage change, from baseline and body weight and a proportion of patients who being 10% or more. The mean change in body weight from baseline was 4.2% for Lybalvi and 6.6% for olanzapine. In the Lybalvi group, 17.8% of patients experienced weight gain that was 10% or more compared with almost 30% in the olanzapine group. Samidorphan is an opioid antagonist and can precipitate opioid withdrawal in patients who are dependent on opioids, which can lead to opioid withdrawal syndrome. Attempts to overcome of all these opioid blockades by administering high or repeated doses of exogenous opioids could lead to life threatening or fatal opioid intoxication. Inform patients of the potential consequences of trying to overcome the opioid blockade and the serious risks of taking opioids concurrently with Lybalvi.

CHARLIE LOVAN, a representative with Janssen AbbVie, brought attention to Braylar though he did not have a testimony. He thanked the committee for the current act.

Ryan Ruggles gave the Magellan presentation on Schizophrenia/Bi-Polar Disorder: Antipsychotics**.** Schizophrenia is the most common psychotic illness, which affects about 1% of population. Between 25% and 50% of schizophrenic patients attempt suicide and 10% succeed. Symptoms include delusions, hallucinations, disorganized speech, catatonic behavior, negative symptoms, and at least one of these should be delusions, hallucinations, or disorganized speech.

Again, guidelines for this class are over a year old, so they will not be reviewed but can be found in the appendix.

Newer guidelines here by the APA in 2020 states that since schizophrenia is a chronic illness that affects all aspects of life. The goals of treatments are to stabilize the patient to return to baseline functioning, prevent recurrence of symptoms, and maximize functioning, and quality of life. Antipsychotics are the standard drugs used in patients with schizophrenia to achieve these goals. They recommend that patients with schizophrenia be treated with an antipsychotic including monitoring of both safety and efficacy. An antipsychotic should be continued in patients whose symptoms improve, with the APA suggesting that the same antipsychotic be used. They recommend clozapine specifically be used in patients with treatment resistant schizophrenia and in patients with a significant risk of suicide. They also suggest clozapine for patients with aggressive behavior despite other treatments. A long acting injectable is suggested for patients who prefer this therapy or for patients with a history of uncertain or poor adherence.

Notably guidelines state that an evidence-based ranking or algorithm approach for antipsychotic selection is not practical due to clinical trial heterogeneity and limited comparative trials. In addition, there's no preference for first generation or second-generation antipsychotics, although clinically many meaningful distinctions such as tolerability do occur. Except for clozapine, no antipsychotic has demonstrated superior efficacy when compared to other agents in the class. And they also state that there is no reliable strategy to predict response. Thus, initial treatment choice is often individualized and includes several patient-specific factors. The guideline also details management of adverse events which is an acute dystonia, parkinsonism, akathisia and tardive dyskinesia, some of which may warrant a switch to an alternative antipsychotic treatment.

Next, we have bipolar disorder. Lifelong prevalence estimates bipolar disorder ranging from 0.9% to 2.1% of the population, characterized by episodes of mania, depression or mixed state. The criterion used to diagnose bipolar I is the presence of manic episode or mixed feature specifiers and three or more other characteristic symptoms. These symptoms include inflated self-esteem or grandiosity, decreased need for sleep, more talkative than usual or pressures speech, flight of ideas or feelings of racing thoughts, distractibility, increase of directed activity or psychomotor agitation and excessive involvement and risky pleasurable activities. This guideline is more than a year old and we will not review. It is here for completeness.

In December 2021 the FDA has approved a new indication for lumateperone for the treatment of depressive episodes associated with bipolar I or II disorder in adults as monotherapy and as adjunctive therapy for lithium or valproate. Lumateperone is already approved for schizophrenia in adults.

In May of 2022 the FDA approved two new strengths of Caplyta 10.5 mg and 21 mg capsules. It was already approved as 42 mg capsules. The new indication is updated as stated. The availability of the 21 mg and 10.5 mg capsules.

In December 2021 the FDA has expanded the indication of brexpiprazole to include treatment of schizophrenia in pediatric patients 13 to 17 years old. Previously brexpiprazole was only

indicated for use in adults. The indication has been updated. Dosage for pediatric patients starts at 0.5 mg per day with a recommended dose of 2-4 mg per day with the maximum dose being 4 mg daily.
And the last slide for antipsychotics, we have utilization were roughly 92.2% was in line with PDL.

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

4-G. MDD: Antidepressants (Green Class); Others Category (Green Class)

MDD: Antidepressants (Green Class)

Ryan Ruggles gave the Magellan presentation on antidepressants. For antidepressants prevalence of 12 month and lifetime, MDD is approximately 21 million American adults or 8.4% of the US population. Women experience depression more often than men. In addition, the prevalence of depression in 2020 was estimated at 4.1 million adolescents. With appropriate treatment, 70% to 80% of patients experiencing MDD achieve 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 handful of 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 of MDD 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.

In terms of treatment resistant depression, it occurs in approximately 20% to 30% of patients with MDD. Although there is no official definition, TRD is often defined as a failure of patients to respond after greater than or equal to two or more treatment attempts of adequate dose and duration of a single depressive episode. In 2019, esketamine nasal spray was approved for TRD and ketamine has been used off label for several years for this purpose, with some data supporting its efficacy. However, standard dosing and approaches have been limited. Although there are no current guidelines specific to TRD, the 2010 APA guidelines state that if there is an adequate response after optimizing the antidepressant dose, for an adequate duration of time, say 4 to 8 weeks, switching to another antidepressant from the same or different class and augmentation with another antidepressant from a different class or non-antidepressant medication are recommended subsequent treatment options.

In addition to psychotherapy, other non-pharm treatment options include transcranial magnetic stimulation, vagus nerve stimulation and ECT. And the APA recommends that ECT should be

considered in patients with MDD that is unresponsive to psychotherapeutic and/or pharmacologic treatment.

In February 2022, the FDA approved citalopram 30 mg oral capsules for the treatment of MDD in adults. Indication as stated. Black box warning includes increased risk of suicidal thoughts and behavior in pediatric and young adult patients taking antidepressants. Closely monitor all antidepressant treated patients for clinical worsening and emergency of suicidal thoughts and behaviors. Pregnancy in SSRI use. Particularly in pregnancy may increase the risk of persistent pulmonary hypertension and symptoms of poor adaption, respiratory distress, temperature and stability feeding difficulties, hypotonia, tremor, irritability in the neonate. Avoid use in patients with hepatic impairment. Avoid use in elderly patients. Recommended dosage of citalopram capsules is 30 mg once daily. Citalopram dosages above 40 mg once daily are not recommended due to the risk of QT prolongation. The availability is 30 mg capsules.

In June of 2022 the indication of postpartum depression has been expanded to include patients greater than or equal to 15 years old. Previously it was only approved for use in adults. The indication has been updated.

In July of 2022, the FDA approved a new form of venlafaxine. Venlafaxine ER. Approval was based on clinical trials of venlafaxine hydrochloride ER capsules. Venlafaxine besylate ER tablets are indicated for the treatment of MDD and generalized anxiety disorder in adults. The indication for MDD and GAD in adults. Warnings are increased risk of suicidal thoughts and behaviors in pediatric and adult patients taking antidepressants. Closely monitor all antidepressant treatment patients for clinical worsening and emergency of suicidal thoughts and behavior. Black box warning states not approved for pediatric patients. In pregnancy, third trimester use may increase the risk of symptoms of poor neonatal adaptation in the neonate. Do not initiate treatment with venlafaxine ER tablets, use another venlafaxine ER product for initial dosage. Titration and dosages below 112.5 mg once daily. Venlafaxine ER tablets can be initiated at 112.5 mg once daily in patients who have received at least 75 mg of another venlafaxine ER product for at least 4 days. Maximum recommended dosage is 225 mg once daily. ER tablet is 112.5 mg.

dextromethorphan and bupropion. In August 2022, the FDA approved the combination of dextromethorphan on competitive methyl-d-aspartate in receptor antagonists and sigma1 receptor agonist and bupropion on amino ketone and CIP 452d6 inhibitor indicated for the treatment of MDD in adults. The indication is as stated. Black box warning includes the increased risk of suicidal thoughts and behavior in pediatric and young adults' patients taking antidepressants. Closely monitor all antidepressant treated patients for clinical worsening and emergency of suicidal thoughts and behaviors. Embryo field toxicity may cause fetal harm. Advise pregnant females of the potential risk to the fetus. Discontinue treatment in pregnancy females and use alternative treatments for females who are planning to become pregnant. Severe renal impairment; not recommended. Severe hepatic impairment; not recommended. Starting dose is 1 tablet once daily in the morning. After three doses increase the maximum recommended dosage of 1 tablet twice daily separated by at least 8 hours. Do not exceed 2 doses in the same day. The availability is 45 mg to 105 mg dextroamphetamine bupropion tablets.

There was a discontinuation of Doxepin in July 2022. A business decision was made to discontinue manufacturing Doxepin 10 mg per ml oral solution.

For antidepressants, both the utilization of motions are broken down by SSRIs and others. For SSRIs, roughly 96% are in line with the PDL.

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

MDD: Others Category (Green Class)

Ryan Ruggles gave the Magellan presentation on Antidepressants Others. The current utilization is roughly 91.8% in line with PDL.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUDIC ALTERNATIVES, SECONDED BY DR. BEGAY-BRUNO. THE MOTION PASSED UNANIMOUSLY.

4-H. Dementia: Alzheimer's Agents

Dementia: Alzheimer's Agents (Red Class)

Public Comments for Dementia: Alzheimer's Agents (Red Class)

JULIA OVERMAN, a representative from Corium spoke about Adlarity. It is indicated for the treatment of Alzheimer's disease. The first area she focused on is the unique characteristics of Adlarity. It is a once weekly transdermal system. It is indicated for the treatment of patients with mild, moderate and severe Alzheimer's disease. Adlarity contains donepezil which was approved in 1996 for the treatment of Alzheimer's dementia. It has demonstrated efficacy in patients with mild, moderate and severe disease. Adlarity is available in two dosage options that are equivalent to 5 mg per day and 10 mg per day. It is designed to provide a reduction in the peaks and troughs of the blood levels that occur with oral medications such as oral donepezil. It is also designed to reduce the adverse events of the GI system as well as the central nervous system that can occur with oral donepezil. It also bypasses the swallowing difficulty that can occur with Alzheimer's disease also known as dysphasia. There is also a reduction in the caregiver burden with a once weekly administration versus daily administration of oral donepezil.

Next, she spoke about the pharmacokinetic profile of Adlarity. In our study when the patches were applied once weekly, they were found to be bioequivalent to oral Aricept that was administered once daily for 35 days. Adlarity retained its skin adhesion during the one-week wear period. Showering did not affect adhesion or the pharmacokinetic parameters.

Finally, she spoke about safety information. Safety assessments revealed that except for abdominal pain patients in the Adlarity group had fewer GI disorders than those in the oral group. The most common GI adverse events were constipation, nausea, diarrhea and abdominal pain. There were also fewer instances of central nervous system side effects such as dizziness

and there were no instances of somnolence with Adlarity use. Adlarity showed good skin tolerability and no patient discontinued early from the study due to skin irritation. No patches were removed due to unacceptable skin irritation. Application site reaction included application site dryness, dermatitis and irritation. For full prescribing information refer to the package insert.

Ryan Ruggles gave the Magellan presentation on Dementia: Alzheimer's Agents. Dementia, characterized by irreversible loss or decline in memory and other cognitive abilities. It affects approximately 6.2 million Americans aged 65 years and older. It is the most common type of dementia accounting for 60% to 80% in the elderly, and it is the sixth leading cause of death in the US. Other types of dementia include vascular dementia, dementia with Lewy bodies, mixed dementia and frontotemporal dementia. Dementia may also be associated with HIV, normal pressure hydrocephalus, Huntington's, Korsakoff, MS, Parkinson's, and Creutzfeldt-Jakob disease. Many other conditions can cause delirium symptoms such as thyroid disorder and vitamin deficiencies but are reversible once the underlying cause is addressed.

Alzheimer's disease, AD, is characterized by progressive cognitive decline associated with the impairment of activities of daily living and behavioral disturbances. Patients with AD eventually lose all cognitive, analytical and physical functioning. 10 warning signs of AD include memory loss that disrupts daily life, challenges in planning or solving problems, difficulty completing familiar tasks, confusion with time or place, trouble understanding visual images and spatial relationships, new difficulties with speaking or writing, misplacement of items or losing the ability to repeat steps, decreased or poor judgement, withdrawal from work or social activities and mood or personality changes. In addition, there are three stages of AD over the course of disease characterized by symptom severity, rate of disease progression and level of necessary support care for activities of daily living.

In March of 2022, FDA approved Adlarity. It is indicated for the treatment of mild, moderate and severe dementia of the Alzheimer's type. Indication as stated. Limitation on pregnancy based on animal data may cause fetal harm. Application site reactions have occurred. Allergic contact dermatitis should be suspended if application site reactions spread beyond the site of the transdermal system. If there is evidence of more intense local reaction and/or if symptoms do not significantly improve within 48 hours after the system is removed. Recommended starting dose is 5 mg per day. After 4-6 weeks the dosage may be increased to the maximum recommended dose of 10 mg per day. If the patient has been on 5 mg per day of an oral treatment for 4-6 weeks or 10 mg per day the recommended starting dose is 10 mg per day. It is available in both 5 mg and 10 mg per day transdermal systems.

On the next slide here, you'll see roughly 92.6% of the utilization in line with PDL.

DR. RYAN MOVED FOR THERAPEUTIC ALTERNATIVES, SECONDED BY DR. LILJEGREN. THE MOTION PASSED UNANIMOUSLY.

4-I. NSAIDs

NSAIDs: (Green Class)

Ryan Ruggles moved directly to utilization for NSAIDS due to it being a green class. In terms of utilization, roughly 99.1% of the utilization is in line with PDL.
DR. DORAN-ATCHISON MOVED THE CLASS EFFECT TO INCLUDE TOPICAL PREPARATION, WHICH WAS SECONDED BY DR. LILJEGREN. THE MOTION PASSED UNANIMOUSLY.

4-J. Opioid Analgesics: Short Acting (Green Class); Long Acting (Green Class)

Opioid Analgesics: Short Acting (Green Class)

Ryan Ruggles gave the Magellan presentation on Opioid Analgesics: Short Acting. Chronic pain is generally defined as pain lasting three -- greater than three months or past the time required for normal tissue healing. It has various etiologies including injury, inflammation, and underlying medical conditions. Approximately 11.2% of adults report daily pain which is greatly misunderstood. Historically, data has suggested that pain may be undertreated, but newer estimates imply that opioid treatments for pain may be over utilized. An estimated 20% of patients presenting to outpatient providers with non-cancer pain or pain-related diagnosis whether acute or chronic receive an opioid prescription.

Likewise, per capita opioid prescription has increased by 7.3% from 2007 to 2012 with prescribers writing 66.5 opioid prescriptions for every 100 Americans in 2016. Unfortunately, approximately 165,000 people have died from overdoses related to opioid pain medications in the US from 1999 to 2014. Likewise, drug-related deaths have tripled from 1999 to 2015, and during 2015 alone, 33,091 people in the US have died from opioid-related overdoses. The overdoses were higher among men being about 13.7% compared to females, which was 7.1%.

Despite this, persistent pain is uncontrolled. If 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 pharm and nonpharmacologic modalities. For postpartum pain the American College of Obstetricians and Gynecologists recommends a step wise multimodal approach to include the use of standard oral pain medications such as acetaminophen, NSAIDs and opioid for post-operative cesarian pain. For vaginal birth a step wise multimodal approach starting with an NSAID or acetaminophen escalating if needed, to an opioid if recommended. ACOG states that if a coating containing medication is selected during duration of therapy a new warn signs of toxicity should be reviewed with the family. If an opioid is required the duration should be limited to the shortest course expected to be adequate for managing acute pain.

In October 2021, the FDA approved an expanded indication for morphine sulfate in pediatric patients weighing 50 kg or more for acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Previously, it was only indicated for acute pain in adults severe enough to require an opioid analgesic for which alternative treatments are inadequate. Because of the risk of addiction abuse and misuse with opioids even at recommended dosage reserve treatment for use in patients who need alternative treatments options. Black box warnings state serious or life threatening or fatal respiratory depression may

occur. Monitor closely, especially during initiation or following a dose increase. There is also a contraindication for children younger than 12 years of age and in children younger than 18 years of age following tonsillectomy and/or adenoidectomy. Avoid use in adolescents 12 to 18 years of age who have other risk factors that may increase their sensitivity to the respiratory depressant effects of tramadol. Initiate treatment with 2 tablets every 12 hours as needed for pain relief. Do not abruptly discontinue in a physically dependent patient. Availability is 56 mg for celecoxib and 44 mg for tramadol, both in tablet form.

There is a new generic for fentanyl (interposing) in August 2022. The generic to Fentora was approved, the buccal sublingual tablet.

On the next and final slide for this about 45.9% was in line with PDL.

Also, to note, the skew was towards non-PDL due to generics. Ryan Ruggles and Charles Semling affirmed this and stated that it would primarily be hydrocodone-acetaminophen tablets and oxycodone tablets.
He also gave a quick disclaimer on the hydrocodone tablets. The reason it is there is because there are two different strengths. There is the 300 mg of acetaminophen and 325 mg of acetaminophen. The 325 mg actually is preferred, but they are all lumped in together under this category, so that number would be much, much higher.

DR. RYAN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNAIMOUSLY.

Long-Acting Opioids: (Green Class)

Ryan Ruggles went directly into utilization on Long-Acting Opioids due to it being a green class.

For utilization 60.5% was in line with PDL.

Dr. Liljegren wanted to know if there was an answer to why there is such a large proportion that are non-PDL prescriptions to which Dr. Semling responded that it is because we do not prefer methadone or oxycontin as those are a majority of the non-PDLs. There are sufficient alternatives for the long-acting. They can also use the medically necessary clause.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS OF THERAPEUTIC ALTERNATIVES, DR. RYAN SECONDED THAT MOTION.

Dr. Liljegren stated she does not feel that methadone should not be used for chronic pain due to it being a dangerous drug.

THE MOTION PASSED BUT WAS NOT UNANIMOUS AS THERE WERE 2 NAYS.

4-K. Neuropathic Pain

Neuropathic Pain: (Green Class)

Ryan Ruggles gave the Magellan went directly to utilization for Neuropathic Pain as this is a green class.

In terms of utilization, roughly 99.1% in line with the PDL.

DR. RYAN MOVED THAT THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. DR. PHILLIPS SECONDED THAT MOTION. THE MOTION WAS PASSED UNANIMOUSLY.

4-L. Anti-Migraine Agents

Anti-Migraine Agents: (Red Class)

Public Comments for Anti-Migraine Agents: (Red Class)

TAMMY MARTIN, a representative from Biohaven Medical Affairs, provided some updated information about Nurtec ODT, also known as rimegepant which is now the first and only migraine medication with a dual indication to both treat and prevent migraine attacks in adults.

Nurtec dissolves within seconds without the need for water. It has a half-life of 11 hours. It also has a migraine specific mechanism of action blocking CGRP. After taking a single dose patients experience pain relief and were functioning normally within 1 hour. Efficacy was sustained through 48 hours without recurrence or redosing.

In a 1-year safety study patients who took rimegepant, as needed, as acute treatment also experienced the benefit of a reduction in migraine frequency over time. A 50% reduction by 32 weeks as well as reduction in the use of other migraine medications like antiemetics and analgesics. A recent real-world analysis has shown that among migraine patients with poor opioid use upon initiation of Nurtec 40% of the patients discontinued opioid use within 9 months. In a double-blind randomized placebo control trial for the preventive treatment of migraine patients took either rimegepant or placebo every other day for 12 weeks. The most common adverse events were nausea in 2.7% and abdominal discomfort in 2.4%. After 12 weeks of every other day dosing rimegepant treated patients demonstrated a significant 4-to-3-day reduction in monthly migraine days which represents 40% reduction in migraine frequency compared to baseline. Importantly, there was a rapid onset of preventive benefit with a 30% reduction in migraine days within the first week of treatment. Until now prescribing preventive treatment for migraine has necessitated polypharmacy because different drugs have been needed to relieve attacks, acute medications, and reduced frequency and severity of attacks preventive medications. Most traditional oral preventative treatments, for example the antihypertensives and antiepileptics and antidepressants, were developed for indications other than migraine. They typically have suboptimal safety and tolerability profiles and adherence is generally poor, less than 20% of patients persist on treatment after 12 months.

Nurtec has a convenient oral administration and a short half-life which may be critical for patients who become pregnant or experience adverse events that might require rapid cessation of drug exposure. Biohaven respectfully asks the committee to consider adding Nurtec ODT as a preferred medication.

CHARLIE LOVAN, a representative from AbbVie, spoke about Qulipta for the patients who suffer with migraine headaches. Qulipta is a calcitonin gene related peptide receptor antagonist indicated for the preventative treatment for episodic migraine in adults. It is available in 10, 30 or 60 mg once daily. Following oral administration Qulipta is absorbed with a peak plasma concentration at approximately 1 to 2 hours and has a half-life of approximately 11 hours. This allows for daily preventive dosing as well as fast clearance of the drug in approximately 3 days.

Qulipta was evaluated in a 12-week phase 3 randomized double-blind placebo-controlled study. The primary endpoint of change or baseline of mean monthly migraine days across 12 weeks compared to placebo was met with all three doses with benefits of Qulipta were evident as early as the first full day after administration. All of the key endpoints were met. These doses significantly improved function as it relates to social and work-related activities. All three doses significantly reduced the mean monthly headache days and the mean monthly acute medication use days by approximately 50%. 55-60% of patients experience at least a 50% reduction of migraine days across the 12-week treatment period. During weeks 9-12 approximately 61-71% of patients experienced a 50% reduction in migraine days.

There is no contraindications, warnings or precautions for Qulipta. The most frequent reported adverse events during the phase 3 trial were constipation, nausea and upper respiratory tract infections. None of the adverse events were considered serious and all reported cases of nausea and most reported cases of constipation were mild or moderate in severity. The discontinuation rate due to nausea, constipation or fatigue were 0.5%.

AbbVie would like to respectfully request that Qulipta be added to the PDL.

ROCHELLE YANG, a representative from Teva, provided some updates on Ajovy. She reminded that Ajovy is a self-injectable subcutaneous CGRP inhibitor and is indicated for the prevention of migraine. It was evaluated in phase 3 randomized controlled trials HALO and FOCUS in episodic and chronic migraine patients. It is the only self-injectable CGRP that is available in both monthly and quarterly dosing.

Earlier this year there were two real-world evidence studies that were published. The first study was a claims database review of 987 patients who were prescribed Ajovy and found a high rate of patient adherence with a mean proportion of days covered or PDC or 86.1% and persistence was found to be more than 75% after 6 months. In the subgroup of patients who had comorbid depression or anxiety at baseline, which are two common comorbidities associated with migraine, there were reductions seen in prescribed antidepressant and anti-anxiolytic medication use respectively. The second study was a retrospective chart study of just over 1,000 migraine patients who had initiated Ajovy and found improvements in clinical outcomes such as the monthly migraine days, monthly headache days, migraine disability assessment questionnaire and headache impact test scores after 6 months. These outcomes were seen in patients regardless

of whether they were on the monthly or the quarterly dosing. This adds to the large body of evidence supporting the use of Ajovy across a broad population of patients with migraine and it is being reviewed today. The committee is asked to add Ajovy to the Alaska State PDL.

Ryan Ruggles gave the Magellan presentation on anti-migraines. In terms of migraine headaches, it accounts for about 10% to 20% of all headaches in adults and affects over 37 million men, women and children in US. It is one of the most common complaints by patients when presenting to a physician, 64% of physician-diagnosed patients who experienced migraines and 41% of undiagnosed migraine sufferers report severe impairment or the need for bedrest due to their migraine symptoms. In addition, 20.7% of women, 9.7% of men experience migraines and epidemiologic profile that has remained stable over the many years. Approximately, 85% of patients with migraine headaches suffer less than three to four attacks per month, and the medium frequency of migraine attacks among migraine sufferers is 1.5 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, pain of moderate to severe intensity. And during the headache, at least one of the following is present; nausea, vomiting, photophobia or phonophobia.

A cluster headache is a severe primary headache disorder characterized by extreme pain on one side of the head and autonomic symptoms, such as nasal congestion and lacrimation. They can persist for weeks to months with a daily or more frequent attacks of 15 to 180 minutes in duration. Yet, estimated lifetime prevalence is more than 1 in 1000 and can either be episodic or chronic in nature with episodic being the predominant form. Individuals with episodic periods of attack followed by periods of remission whereas individuals with chronic have minimal to no periods of remission between headache attacks.

In September 2021, the FDA approved Trudhesa, which is a dihydroergotamine mesylate 4 mg/mL nasal spray, approved for the acute treatment of migraine with or without aura in adults. The limitation for this, it is not indicated for preventative treatment of migraines or for the management of hemiplegic or basilar migraine. There is a black box warning where severe, serious and/or life-threatening peripheral ischemia has been associated with co-administration with strong CYP3A4 inhibitors, because the inhibitors elevate the serum levels of this medication, the risk of vasospasm leading to cerebral ischemia and/or ischemia of the extremities is increased. Hence, concomitant use of this medication is strong, so 3A4 inhibitors is contraindicated. There is a warning for pregnancy where based on animal data, it may cause fetal harm. Avoid use in patients with severe hepatic impairment, severe renal impairment or end stage renal disease. Dose adjustment of 10 mg once daily is required in those patients.

For dosage, recommended dose is 1.45 mg, which is administered as one-metered spray of 0.725 mg into each nostril. The dose may be repeated if needed a minimum of one hour after the first dose and one should not use more than two doses within 24 hours or three doses in seven days. It is available as a nasal spray.

In October 2021, FDA approved Qulipta which is a CGRP antagonist indicated for the preventative treatment of episodic migraines in adults. In terms of warnings, based on animal data, it may cause fetal harm and to avoid in patients with severe hepatic impairment. The dosage is 10, 30 and 60 mg taken orally once daily with or without food, and there is a dose adjustment for patients with severe renal impairment or end-stage renal disease. And again, it is available in tablet formulation in 10, 30 and 60 mg. Lastly, there was a new generic in October 2021 for zolmitriptan. FDA approved the first generic of AstraZeneca Zomig nasal spray from Padagis, Israel.

For triptans, approximately 96.6% was in line with the PDL.

DR. RYAN MOVED THE DRUGS BE CONSIDERD A CLASS EFFECT TO INCLUDE AT LEAST ONE NON-ORAL PREPARATION, AT LEAST ONE DRG FOR ACUTE TREATMENT AND A DRUG FOR PROPHYLACTIC TREATENT. DR. PHILLIPS SECONDED THAT. THE MOTION PASSED UNANIMOUSLY.

DR. PHILLIPS MOVED THAT THE ANTI-MIGRAINE AGENTS BE CONSIDERED AS A THERAPEUTIC ALTERNATIVE FOR ACUTE AND PROPHYLACTIC TREATMENT. DR. LILJEGREN SECONDED THAT. THE MOTION PASSED UNANIMOUSLY.

The group took a 10-minute bio break.

4-M. Skeletal Muscle Relaxants

Skeletal Muscle Relaxants: (Blue Class)

Ryan Ruggles gave the Magellan presentation on Skeletal Muscle Relaxants. Skeletal muscle relaxants, spasticity, a condition in which muscles are continuously contracted causing stiffness or tightness which may interfere with movement and speech. It is usually caused by damage to a portion of the brain or spinal cord that controls voluntary movement. It is a major health concern and can be associated with a number of disease entities such as spinal cord injury, MS, TBI, cerebral palsy and stroke. Symptoms may include hypertonicity, clonus, exaggerated deep tendon reflexes, muscle spasms, scissoring and fixed joints. The degree of specificity varies from mild muscle stiffness to severe painful and uncontrollable muscle spasms. Specificity may cause decreased range of motion, contractures, sleep disorders and impaired ambulation. Skeletal and muscle relaxants are FDA approved to treat two different types of conditions. Muscular pain or spasms from peripheral and musculoskeletal conditions or specificity from upper motor neuron syndromes. Both conditions affect patients' ability and affect independence and activities of daily living and work.

December 2021, the FDA approved a new oral granule formulation of baclofen. Baclofen is indicated for the treatment of specificity resulting from MS, particularly, for the relief of flexor spasms and concomitant pain, clonus and muscular rigidity and may also be of some value in patients with spinal cord injuries and other spinal cord diseases. The indication is for the treatment of specificity resulting from MS, particularly for the relief of flexor spasm and

concomitant pain, clonus and muscular rigidity. It may also be of some value in patients with spinal cord injuries and other spinal cord diseases. Limitations of use are that it is not indicated for the treatment of skeletal muscle spasm resulting from rheumatic disorders. Because baclofen is excreted unchanged through the kidneys it may be necessary to reduce dosage in patients with impaired renal function. Pregnancy, based on animal data, may cause fetal harm. Initiate with a low dosage, preferably in divided doses, administered orally and increase gradually based on clinical response and tolerability. The maximum oral dosage is 80 mg daily, which would be 20 mg four times a day. The availability is oral granules 5, 10, 20 mg baclofen and comes in a packet.

February 2022, the FDA approved a new formulation of baclofen. Fleqsuvy is an oral suspension for the treatment of spasticity resulting from MS, particularly, for the relief of flexor spasms and concomitant pain, clonus and muscular rigidity and may also be of some value in patients with spinal cord injuries and other spinal cord diseases. Indication as per stated. It is not indicated for the treatment of skeletal muscle spasm resulting from rheumatic disorders. Renal and pregnancy indications are the same as the prior slide. Initiate with a low dosage, preferably in divided doses with the maximum being 20 mg 4 times a day. Oral suspension is 25 mg per 5 ml.

There was a recall on orphenadrine citrate in March 2022. It was a voluntary recall that recalled 13 lots of orphenadrine citrate 100 mg ER tablets to the consumer level. It was due to the presence of nitrosamine impurity above the acceptable daily level.

The utilization where roughly 97.8% is in line with PDL.

DR. LILJEGREN MOVED THAT THE DRUGS ARE THERAPEUTIC ALTERNATIVES EXCLUDING CARISOPRODOL FROM THE PDL. TRISH WHITE SECONDED THE MOTION. THE MOTION PASSED UNANIMOUSLY.

4-N. Restless Legs Syndrome

Restless Legs Syndrome: (Green Class)

Ryan Ruggles gave the Magellan presentation on Restless Legs Syndrome. Given that this is a green class they went right into utilization which was found to be 100% non-PDL. This is due to this class being combined into other classes. If only RLS drugs that were on the PDL the utilization would be 93.2% on PDL at 6 hundred and (interposing) prescriptions.

DR. RYAN MOVED THE DRUGS TO CLASS EFFECT, DR. LILJEGREN SECONDED THAT. THE MOTION WAS PASSED UNANIMOUSLY.

4-O. Smoking Cessation

Smoking Cessation: (Green Class)

Ryan Ruggles gave the Magellan presentation on Smoking Cessation. Given that this is a green class they went directly to utilization which 96.9% was in line with the PDL.

DR. LILJEGREN MOTIONED THAT THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, WHICH WAS SECONDED BY DR. DORAN-ATCHISON. THE MOTION WAS PASSED UNANIMOUSLY.

4-P. Opioids: Opioid Dependence (Green Class); Reversal Agents (Blue Class)

Opioid Dependence: (Green Class)

Ryan Ruggles gave the Magellan presentation on Opioid Dependence. Given this is a green class they went directly to utilization. He stated that utilization where roughly 90.9% is in line with the PDL.

DR. LILJEGREN MOVED THAT THE DRUGS ARE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE LONG-ACTING INJECTABLE PRODUCT. DR. PHILLIPS SECONDED THAT MOTION. THE MOTION WAS PASSED UNANIMOUSLY.

Reversal Agents: (Blue Class)

Ryan Ruggles gave the Magellan presentation on Reversal Agents. There is an estimated 37.3 million Americans aged 12 years and older who were current in the past month illicit drug users. There were approximately 9.4 million people aged 12 years or older in the US who misused opioids in the past year, approximately 40.3 million aged 12 years or older in 2020 were considered to have a substance use disorder including 18.4 million with an alcohol use disorder, 2.7 million with an illicit drug use disorder and 1.6 million had an opioid use disorder.

US Preventive Task Force in 2020 issued a final recommendation statement on screening for unhealthy drug use. For adults, they recommend screening implemented when services for accurate diagnosis, effective treatment and appropriate care can be offered or referred. For adolescents, the current evidence is insufficient to determine the benefits and harms of screening for unhealthy drug use.

In October 2021, FDA approved a new formulation of naloxone an opioid antagonist indicated in adult and pediatric patients for the emergency treatment of known or suspected opioid overdose as manifested by respiratory and/or CMS depression. It is intended for immediate administration as emergency therapy in settings where opioids may be present and is not a substitute for emergency medical care. There is a risk of recurrent respiratory and CNS depression. Due to the duration of action naloxone relative to the opioid keep the patient under continued surveillance and administer repeat doses of naloxone using a new nasal spray with each dose necessary while awaiting emergency medical assistance. There is risk of limited efficacy with partial agonists or mixed agonist antagonist reversal of respiratory depression caused by partial agonist or mixed agonist antagonist such as buprenorphine and pentazocine may be incomplete. Dosage; seek emergency medical care immediately after use. Administer to adult or pediatric patients into the anterior lateral aspect of the thigh through clothing if necessary. Keep the patient under continued surveillance until emergency personnel arrive and administer repeated doses as

necessary. Availability is injection 5 mg per 0.5 ml naloxone solution in a single dose prefilled syringe.

In October 2021, FDA approved a naloxone injection, 10 mg by use of military personnel and chemical incident responder for emergency treatment of patients greater than or equal to 12 years of age where use of high potency opioids, such as fentanyl analogs as a chemical weapon is suspected and for temporary prophylaxis of respiratory and/or CNS depression in military personnel and chemical incident responders entering an area contaminated with high potency opioids such as fentanyl analogs.

Moving onward to the utilization 100% in line with PDL

Dr. Semling stated that the 100% utilization may be a little misleading because when looking at the utilization sheets it only had Narcan nasal spray on there. On the current PDL there are multiple alternatives.

DR. LILJEGREN MOTIONED THAT THE DRUGS IN THE CLASS ARE THERAPEUTIC ALTERNATIVES. DR. RYAN SECOND THAT MOTION. THE MOTION WAS PASSED UNANIMOUSLY.

4-Q. RSV Monoclonal Antibodies: (Green Class)

Ryan Ruggles gave the Magellan presentation on RSV Monoclonal Antibodies. Given that this is a green class he moved directly to utilization stating that there was none.

Dr. Semling stated that was not true and that the slide should be relook at the slide. Synagis, for RSV, is what they looked at and it is 100 preferred and utilization is 100%. With the uptick in RSV this year around the country and Alaska the RSV team, including himself, met and opened up the RSV Synagis season early due to the rise in case numbers. Utilization is 100%.

After some discussion it was found that the data was pulled prior to Synagis season.

DR. RYAN MOVED THE CLASS EFFECT. DR. LILJEGREN SECONED THAT MOTION. THE MOTION WAS PASSED UNANIMOUSLY.

5. Review Minutes from the September meeting

There were no changes to the meeting minutes.

DR. RYAN MOVED TO APPROVE THE MEETING MINUTES OF *. SECONDED BY DR. PHILLIPS. THE MOTION WAS PASSED BY ALL MEMBERS.**

6. End of Public Meeting

7. Comments From Committee Members

8. Adjourn

DR. SEMLING MOVED TO ADJOURN THE MEETING. THE NEXT MEETING WAS SCHEDULE FOR JANUARY 20, 2023. WITHOUT OBJECTION, THE MEETING WAS ADJOURNED.