Alaska Medicaid Pharmacy and Therapeutics Meeting

MINUTES OF MEETING
November 19, 2021

Committee Members Present:
John Riley, PA, Acting Chairman
Robert Carlson, MD
Diane Liljegren, R.Ph.
Sarah Doran-Atchison, PharmD
Claudia Phillips, MD
Jonathan Harrison, PharmD
Charles Ryan, MD

Committee Members Absent:
Trisha White, R.Ph.

Others Present:
Umang Patel, Pharm D, R.Ph., Magellan Medical Administration
Charles Semling PharmD, DHSS
Erin Narus PharmD, MSJ, DHSS
Ryan Norman, Pharm D, MBA, Teva Pharmaceuticals
Margaret Olmon, PharmD, AbbVie
Desiree Crevecoeur-MacPhail, ICMA Pharmaceuticals
Lisa Allen, Vertex Pharmaceuticals
Shirley Quach, Novartis Pharmaceuticals
Linda Finch, Biogen
Matthew Clark, Zogenix
Kristen Heard, Neurelis
Tim Bernard, Alkermes
Sophia Yun, Janssen
Payal Tejani, Indivior

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)

Dr. Umang Patel gave the Magellan presentation for Cystic Fibrosis: CFTR potentiator class. Cystic fibrosis is a serious autosomal recessive multi organ disorder. It affects approximately 32,000 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 48 years with 80% reaching adulthood. Children are anticipated to live to approximately 40 years of age with current treatments, and in 2019 adults comprised about 56% of the CF population, while in 1988, they comprised approximately 31%. Mutations lead to the disease of the exocrine gland function resulting in the formation of a thick mucus that builds up in the lung, 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. The goals of treatment are one, maintaining lung function by controlling infections or mucus; two, maintaining appropriate growth by providing nutritional support; and three 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's 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 December 2020, the PI updated to expand the indication to include patients with cystic fibrosis who have a mutation in the CFTR gene that is responsive based on in vitro data. Updated indication, treatment of cystic fibrosis in patients aged 12 years or older who have one or more F508del mutation in the CFTR gene, or a mutation with CFTR gene that is responsive based on in-vitro data.

In June 2021, the FDA approved Trikafta for the treatment of cystic fibrosis in patients age 6 through 11 years old, with at least one F508del mutation that are responsive to in-vitro data. And additionally, in the same time, they approved a new dosage containing 50 mg of Elexacaftor, 25 mg of Tezacaftor, 37.5 mg of Ivacaftor co-packaged with Ivacaftor 75 mg to accommodate the new dosage of the new age group. The updated indications and the updated availability were the only changes to Trikafta in the last year.
here, we have the utilization 100% is in line with PDL. Previous year's motion, Dr. Phillips moved the drugs in the class were therapeutic alternatives, to be used appropriately seconded by Dr. Carlson and passed unanimously.

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

LISA ALLEN, a representative of Vertex Pharmaceuticals, provided public testimony on behalf of Vertex CFTR modulators. The CFTR modulators are the only CF medicines that work by targeting the underlying cause of CF, which is a defect in the CFTR protein. There are currently four CFTR modulators approved for treatment of CF based on age and genotype - Trikafta, Symdeko, Orkambi and Kalydeco. There have been several label updates and expansions to these products labels, including the additional CFTR mutations for the three Vertex medicines, Trikafta, Symdeko and Kalydeco that were approved in December 2020. These additional mutations were approved based on in-vitro data from an established cell model system that can be used to treat rare CFTR mutations for responsiveness to CFTR modulators, when clinical trials are not feasible due to low patient numbers.

In addition, the FDA expanded the use of Trikafta to include the patients with CF age 6 to 11, who have at least one F508del mutation or mutation in the CFTR gene that was responsive. An additional warning and precautions were updated in October of this year. Section 6.2 post-marketing experience was added to the Trikafta USPI and section 5.1 warnings and precautions were updated as follows: Liver failure leading to transplantation has been reported in a patient with cirrhosis and portal hypertension, while receiving Trikafta. Avoid the use of Trikafta in patients with preexisting advanced liver disease, as evidenced by cirrhosis, portal hypertension, ascites or hepatic encephalopathy, unless the benefits are expected to outweigh the risks.

If used in these patients, they should be closely monitored after the initiation of treatments. Isolated elevations of transaminases or bilirubin have been observed in patients with CF treated with Trikafta. In some instances, transaminase elevations have been associated with concomitant elevation in total bilirubin and/or the international normalized ratio or INR and have resulted in patients being hospitalized for intervention, including patients without a history of pre-existing liver disease. Refer to the full prescribing information for a complete list of warnings and precautions associated with these modulator as well as additional safety data.

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

Cystic Fibrosis: Inhaled Antibiotics (Green Class)

Dr. Umang Patel gave the Magellan presentation for Cystic Fibrosis: Inhaled Antibiotics. There were only about five units in the last three months. They were not in line with PDL. Previous year's motion stated Mr. Riley moved the drugs from the class were therapeutic alternatives, seconded by Dr. Phillips and passed unanimously.

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

Cystic Fibrosis: Pancreatic Enzymes (Green Class)

Dr. Umang Patel gave the Magellan presentation for Cystic Fibrosis: Pancreatic Enzymes. The utilization report was reviewed and stated that they are roughly 95% is in line with the PDL. Previous year's motion Dr. Phillips moved the class effect, seconded by Miss White and motion passed unanimously.

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

4-B. MS Agents: CNS Therapeutic Classes

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

SHIRLEY QUACH, a representative from Novartis Pharmaceuticals provided some information about Kesimpta as part of the review. Kesimpta was FDA approved in August of last year for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing remitting disease and active secondary progressive disease in adults. Kesimpta is the first fully human anti CD20 monoclonal antibody for targeted B-cell therapy in RMS. And it offers the advantage of being self administered once a month at home with a Sensoready autoinjector pen. Other anti-CD20 monoclonal antibodies are administered by IV infusion.

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. Kesimpta offers providers a highly efficacious MS agent with a favorable safety profile via a monthly self administered injection. In the two pivotal Kesimpta trials published in the New England Journal of Medicine, all Kesimpta endpoints reaches statistical significance versus teriflunomide. The annualized relapse rates for patients, this was the primary endpoint. For those patients on Kesimpta, it reduced from a baseline of 1.2 relapses per year to 0.10 or roughly 1 relapse every 10 patient years. And the safety profile for Kesimpta was similar to teriflunomide. And based on a network meta-analysis published in 2020, Kesimpta is considered to be a high efficacy DMC in regards to the primary endpoint of ARR.

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.

LINDA FINCH, a representative from Biogen, spoke 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 that of Tecfidera or dimethyl fumarate,

but it is converted to the same active metabolite monomethyl fumarate, and because it's bioequivalence, we can expect to see the same efficacy and safety as Tecfidera, which has now been prescribed in over 425,000 patients and represents over 810,000 patient years of experience.

The 10-year data from the long term endorsed trial was recently reported. 73% of patients had 0 or 1 relapse and over 50% had 0 relapse in 10 years. And also importantly, 64% had no progression and disability. Vumerity has been studied for improved patient reported gastrointestinal tolerability versus Tecfidera. There are two distinct Vumerity studies called EVOLVE-MS-1 and EVOLVE-MS-2. EVOLVE-MS-1 is an ongoing 96-week open label single arm phase 3 study assessing long term safety and tolerability as well as exploratory efficacy of Vumerity in patients with relapsing remitting MS. In a pre specified interim analysis, 30% of patients had a GI adverse event, but most were mild to moderate and less than 1% discontinued due to GI adverse events. The other study EVOLVE-MS-2 is a phase 2 randomized, active controlled five-week head to head study that evaluated patient reported GI tolerability for Vumerity versus Tecfidera in relapsing remitting MS patients.

Patients treated with Vumerity experienced a statistically significant improvement in a patient reported outcome measuring GI adverse events symptom intensity. Adverse events, leading to study discontinuation were reported in 1.6% of Vumerity patients versus 6% of Tecfidera patients. And the GI discontinuation rates were 0.8% for Vumerity versus 4.8% for Tecfidera. And then recently published real world data that was presented last month has reinforced that patients are highly adherent to Vumerity, consistent with expectations based on the clinical trial data. The most common adverse reactions for dimethyl fumarate, which has the same active metabolite as Vumerity, are flushing, abdominal pain, diarrhea and nausea. And Vumerity's warnings and precautions are the same as for DMF.

MS is a heterogeneous disease and patients present with a variety of symptoms and variable disease progression. And then this progressive illness, it's important to have access to the appropriate medication as early in the disease as possible to prevent relapse and disability progression. And the oral disease modifying therapies are very different medications with different MLAs, different tolerability profiles, monitoring requirements, drug interactions, and different contraindications and all of these factor into appropriate drug selection.

Umang Patel 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 February 2021, the FDA approved an IM route of administration of Plegridy and the corresponding prefilled syringe. Dosage as the same as the subcutaneous formulation, which is about 125 mcg per 0.5 mL every 14 days. Patients may self-administer IM injections with proper training, switching between subcutaneous and IM routes administration and vice versa has not been studied. The need for repeat of dose titration is not expected when switching routes. And again, there's no changes that indication limitations or dosage, just a new availability.

In March 2021, FDA approved a new medication called Ponvory which is 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 adults. There are some limitations here. There could be possible liver injury, increased blood pressure, cutaneous malignancies, fetal risk for women of childbearing potential and hepatic impairment. There's a titration that is required. The recommended maintenance dose is about 20 mg, once daily, and it is recommended to monitor the patients for sinus bradycardia first degree or second degree AV blocks or history of MIs or heart failure. And the availabilities are in various strengths ranging from 2 mg to 20 mg tablets here.

Regarding Lemtrada, in June 2021, multiple modifications to the REMS program including updating the REMS material to align with labeling changes from September 2020, updates to allow for online enrolling of patients, phase 2 allow pharmacies to receive authorizations for shipping the product online. The infusion checklist was updated and aligned with the REMS material. Certain REMS materials were consolidated to remove redundancy and update in timeframe for returning unused vials. A new REMS documents was added.

The utilization showed that roughly 56% was in line with PDL. Previous year's motion, Dr. Phillips moved the drugs in the class were therapeutic alternatives, which was seconded by Dr. Carlson and passed unanimously.

DR. LILJEGREN MOVED THAT THE DRUGS WERE THERAPEUTIC ALERNATIVES, SECONDED BY DR. DORAN ATCHINSON. THE MOTION WAS PASSED UNANIMOUSLY.

4-C. ADHD: Stimulants and Related Agents

ADHD: Stimulants and Related Agents (Green Class)

Umang Patel 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 Pitocin and [Indiscernible 37:56] were not addressed by the medical letter.

Hypersomnolence is excessive sleepiness. It is the primary and often debilitating symptom experienced by adults with narcolepsy, obstructive sleep apnea and shift work sleep disorder. The defining characteristic is a consistent inability to stay awake and alert enough to safely and successfully accomplish tasks of daily living. Persons experiencing excessive sleepiness, who seek medical attention typically complain of fatigue, tiredness, lapses of attention, lack of energy, low motivation, difficulty concentrating, disruptive sleep, snoring or difficulties at work.

In October 2020, the FDA approved expanded indication for Wakix for treatment of cataplexy in adults with narcolepsy. It was already indicated for treatment of excessive daytime sleepiness. Again, no changes to any warnings and precautions, dosage or availability, just an added indication here.

In March 2021, the FDA approved a new medication Azstarys for the treatment of ADHD in patients 6 years of age or older. There is a black-box warning CNS stimulants and class black-box warning have a high potential for abuse and dependence, assess the risk of abuse prior to prescribing and monitor for signs or symptoms of abuse and dependence while on therapy. And there is warning for serious CB reactions as well. The dosing is stratified by age, pediatric patients defined as ages 6 to 12 years of age and pediatric patients 13 to 17 years and adults are on stratified dosing regimens as you can see here. And it is recommended to not substitute for

other methylphenidate products on a milligram-to-milligram basis. The availability of this medication are capsules since this is a combination of two medications. As you can see that it is a combination of the two. In terms of pregnancy for this medication, there are no available data to evaluate drug associated risk of major birth defects. And there is no experience in patients of renal or hepatic impairment with this medication to provide a recommendation on dosing adjustments.

In April 2021, the FDA approved Evekeo ODT for the treatment of ADHD in pediatric patients 3 to 17 years of age. Previously, it was only approved for children 6 years or older. And at that same time, they also approved new 2.5 mg ODT strength, and it was already approved for 5, 10, 15 and 20 mg. No changes in terms of warnings. Again, the indication was now extended over to 3 years of age or older. Dosing similar to the previous slide is stratified by age. And the new availability is seen there as well for 2.5 mg.

In April 2021, the FDA approved Qelbree for ADHD, in pediatric patients 6 to 17 years of age. In clinical trials higher rates of suicidal thoughts and behavior reported in pediatric patients treated with Qelbree than in patients treated with placebo closely monitor for worsening and emergence of suicidal thoughts and behavior. There are other precautions for blood pressure and heart rate increase, activation of mania or hypomania. There is precautions with patients who are of childbearing age, and there it is not recommended in patients with hepatic impairment here. The dosing again stratified by patients who are 6 to 11 years of age or 12 to 17 years of age. And the availability is in extended-release capsules, ranging from 100, 150 and 200 mg strength.

There was a recall in April 2021 for guanfacine extended release. Apotex issued a voluntary recall of three lots in 2 mg to the consumer level due to trace amounts of quetiapine fumarate in one lot. Out of caution, two other lots were also recalled. No adverse effects were reported in this recall, but exposure in trace amounts could result in hypersensitivity reactions. In addition, exposure to quetiapine could result in additive effects in lowering blood pressure, sleepiness and sedation and possibly dizziness as well.

We have the utilization where roughly 98% is in line with the PDL. Previous year's motion Dr. Phillips moved the drugs in the class were therapeutic alternatives to include at least one oral preparation, one extended-release preparation, one nonstimulant preparation, when alpha agonist and one ODT as orally disintegrating preparation or liquid. This was seconded by Mr. Riley and passed unanimously.

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

4-D. Insomnia: Sedative Hypnotics

Insomnia: Sedative Hypnotics (Blue Class)

Umang Patel 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 terms of guidelines, the US Department of the Veterans Affair and DOD in 2020 published guidelines on management of patients with chronic insomnia disorder obstructive sleep apnea that provides 3 one-page algorithms and 41 recommendations around diagnosis and assessment of OSA and chronic insomnia disorder, treatment and management of chronic insomnia disorder.

In terms of obstructive sleep apnea, positive airway pressure is recommended as well as caution or avoidance of opioids and sedative hypnotics. And in terms of chronic insomnia, cognitive behavioral therapy is recommended first line. The weaker recommendations are given for low dose doxepin, zolpidem, Zaleplon or eszopiclone at the lowest effective dose for the shortest possible duration. There's insufficient evidence to recommend four against Tasimelteon or suvorexant. They also recommend against use of herbal supplements, antipsychotics, benzos, and diphenhydramine as well.

In December 2020, the FDA approved a new indication for Hetlioz and Hetlioz LQ for the treatment of nighttime sleep disturbances in Smith-Magenis Syndrome in pediatric patients 3 to 15 years of age. As you can see, they already had other indications. No changes to limitations or availability. And due to this new indication, the pediatric dosing was updated and it's stratified by age and weight as well. In terms of patients who are of reproductive potential, available post

marketing case reports with this medication in pregnant women are not sufficient to evaluate drugs associated risk of major birth defects.

Roughly about 71% of prescriptions were in line with the PDL. Previous year's motion Mr. Riley moved the drugs in the class were therapeutic alternatives, seconded by Dr. Phillips and passed unanimously.

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

4-E. Epilepsy: Anticonvulsants

Epilepsy: Anticonvulsants (Blue Class)

Public Comments on Epilepsy: Anticonvulsants

MATTHEW CLARK, a representative of Zogenix, discussed Fintepla. He stated that in his prior presentation to the committee, we presented the safety and effectiveness of Fintepla for the treatment of seizures associated with Dravet Syndrome. Safety and effectiveness was established in two randomized double blind placebo controlled trial. Fintepla oral solution was approved by the FDA on June 25, 2020, and is indicated for the treatment of seizures associated with Dravet Syndrome in patients two years of age and older. Dravet Syndrome is a rare and severe form of epileptic and developmental encephalopathy that is highly refractory to existing anticonvulsant therapy.

At the most recent annual meeting of the American Epilepsy Society, results of a third phase three study of Fintepla were reported. Study three was another randomized double blind placebo controlled trial of 143 Dravet patients whose seizures were not adequately controlled by existing anticonvulsants. In the 0.7 mg/kg/day group there was a 64.8 greater reduction in mean monthly convulsive seizure frequency and a 49.9 greater reduction in the 0.2 m/kg/day group compared with placebo. Fintepla was generally well tolerated with an adverse event profile consistent with those observed in study one and study two and no observations of valvular heart disease or pulmonary arterial hypertension.

Data from an ongoing analysis, entitled efficacy and tolerability of adjunctive Fintepla and an open label extension study on Dravet Syndrome patients treated for up to three years was reported. Patients who successfully completed study one, two or three were eligible. In the interim analysis 330 enrolled patients had a median treatment duration of 631 days. In this study Fintepla provided a sustained clinically meaningful reduction in median monthly convulsive seizure frequency with a minus 65% reduction observed over the course of the entire open label extension period. Additionally, 63% of the patients had a clinically meaningful or greater than 50% reduction in monthly convulsive seizure frequency, while 38% had a profound or greater than 75% reduction. Most common treatment emergent adverse events were pyrexia, nasal pharyngitis, decreased appetite, increased blood glucose, upper respiratory tract infection, diarrhea and seizure. No cases of valvular heart disease or pulmonary hypertension were observed.

KRISTEN HEARD, a representative from Neurelis, spoke about Valtoco. Valtoco, an intranasal diazepam formulation for emergency rescue treatment of seizure clusters is the first and only intranasal rescue treatments for patients with epilepsy at age 6 years and older. A clinical trial to investigate the safety and pharmacokinetics of Valtoco in children aged 2 to 5 is underway with the goal of possible label expansion.

Valtoco efficacy is based on the relative bioavailability of Valtoco compared to diazepam rectal gel Diastat. And diazepam efficacy in seizure cluster has been established. Valtoco was designated clinically superior to Diastat by the FDA. Patients live with a burden of not knowing when seizure clusters will occur. The goal of rescue medication is to treat the active seizure and subsequently terminate the cluster once recognized. Seizure clusters are commonly defined as two or more seizures within 24-hour period. And a recent analysis of patients' diaries show that the majority of seizure events within the cluster tend to occur between 6 and 24 hours after the possessing seizure. Valtoco which has a life of a half life or 49.2 hours would allow coverage within the expected 24-hour timeframe of a seizure cluster. That's how this proprietary excipient interval increases drug absorption across the nasal mucosa resulting in 97% bioavailability relative to IV diazepam. Other PK parameters are two to four fold less variable for Valtoco than Diastat.

For dosing, dosing is based on patient's age and weight with 5, 10, 15 and 20 mg doses available. The clinical development program consists of five studies including a long term safety study. Findings from that safety study were consistent with what is known for diazepam and the rate of somnolence was 1.8%. And exploratory analysis showed subjects with epilepsy and their caregivers reported treating almost 4,000 seizure events, 94% use a single dose of Valtoco over a 6-hour period and 87% used a single dose over a 24-hour period. Valtoco has a black-box morning as to all benzodiazepines regarding concomitant use of opioids, abuse, misuse and addiction and dependence in withdrawal reactions. The most common local adverse events are nasal discomfort, nasal congestion, epistaxis and dysphasia. And for additional important safety information, you could please see the full prescribing information for Valtoco.

In summary, Valtoco provides a non invasive on-hand rescue treatment for these seizure emergencies and is the only nasal spray indicated in patients 6 and above. Valtoco is designated clinically superior to Diastat by the FDA, and the availability of rescue medications easily administered at home or out of the hospital has the potential to decrease unnecessary utilization of healthcare resources, break the cycle of seizures and prevent progression to status epilepticus. I am happy to take any questions you may have.

Umang Patel 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.

First medication, here we have Vimpat. In November 2020, FDA approved an expanded indication for the adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in patients 4 years of age or older, was previously only indicated for treatment of partial onset seizures in patients 4 years of age or older. Again, no changes to any of the warnings or availabilities. There's a new dosage here. Dose adjustment for 50 mg twice daily, and for pediatric patients less than 17 years of age, it is weight based. In terms of pregnancy data, based on animal data, this medication may cause fetal harm. And there is dosage adjustment required for severe renal impairment and it is not recommended for severe hepatic impairment.

On the next slide here we have Spritam. In January 2021, FDA approved an expanded indications for the treatment of partial onset seizures in patients 4 years of age or older weighing over 20 kg. It was previously indicated as adjunctive therapy in patients with epilepsy 4 years of age or older weighing over 20 kg. Again, no updates or changes here for any of the warnings, dosage or availability. There is a dose adjustment required for mild, moderate and severe renal impairment, but there is no dose adjustment for any hepatic impairment here.

Next, we have an FDA communication for Lamotrigine. And this is relevant to all subsequent brand names Lamictal, Lamictal CD, ODT, and XR. So in April of 2021, FDA issued a drug safety communication regarding a potential increase of arrhythmias in patients with heart disease as a result of reports of abnormal ECGs. FDA will continue to evaluate and inform the public and healthcare professionals of their findings as more required in-vitro studies are available. Healthcare practitioners should assess whether the potential benefits of Lamotrigine outweigh the potential risk of arrhythmias in each patient.

Lastly, we have a new medication here, Broviac. And in September 2021, FDA approved an expanded indication for the treatment of partial onset seizures to include pediatric patients 1 month to less than 4 years for tablets and oral solution and expanded the patient population to include pediatric patients 1 month to less than 16 years for injection when oral administration is temporarily not feasible. No changes to any of the warnings. Based on animal data, it may cause fetal harm. The dosing is stratified by age as you can see here. In terms of specialized populations, dose adjustment is recommended for all stages of hepatic impairment. And it is not required for patients with impaired renal function.

When we look at utilization, you can see about 94% is in line with a PDL. Previous year's motion, Dr. Phillip moved the drugs in the class were therapeutic alternatives, which was seconded by Mr. Riley and passed unanimously.

DR. RYAN 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

TIM BERNARD, 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.

SOPHIA YUN, a representative with Janssen Scientific Affairs Value and Evidence team spoke on behalf of Invega Hafyera, also known as six months paliperidone palmitate extended release injection. Invega Hafyera was approved by the FDA on 08/30/21 for the treatment of schizophrenia in adults after they have adequately been treated with either Invega Sustenna for at least four months or Invega Trinza following at least 1 three-month injection cycle. Prescribing information can be referred to for complete clinical information. The is also a black box warning regarding elderly patients with dementia related psychosis treated with antipsychotic drugs are at an increased risk of death.

A phase three randomized double blind active controlled parallel group multicenter non-inferiority trial was conducted to evaluate the efficacy and safety of Invega Hafyera. And the time to first relapse in adults with schizophrenia were previously stabilized on corresponding doses of Sustenna or Trinza. Invega Hafyera demonstrated a non-inferiority to Invega Trinza on the primary endpoint at first time to relapse at the end of the 12-month double blind phase in the intent to treat analysis. In the intent to treat analysis, 7.5% of patients in the Invega Hafyera treatment group and 4.9% of patients in the Invega Trinza group experienced a relapse event.

The safety profile of Invega Hafyera was generally consistent with the previous studies of Sustenna and Trinza. Long acting injectables are recommended for schizophrenia patients who are not adherent, partially adherent or frequently relapsing in the response to therapy or when patient's environment is that an LAI is more reliable route of administration. Several guidelines such as the US Veterans Affairs or the University of South Florida recommend that LAI should be used in patients with a preference for LAIs.

In a meta-analysis inclusive of randomized controlled trials, cohort studies and pre post studies comparing LAIs to oral antipsychotic and patients with schizophrenia, LAI has demonstrated reduced risk of relapse or hospitalization with no significant difference in reported adverse events. LAI use was also associated with lower hospitalization rates, fewer hospitalization days and decreased healthcare resource use and improved adherence compared to oral antipsychotics. As schizophrenia requires highly individualized patient care with such devastating consequences with associated with relapse, we respectfully request that the Alaska State P&T board add Invega Hafyera to the preferred drug list as you have with Invega Sustenna and Trinza to provide access to this unique once every six-month antipsychotic as an option for Alaskans.

PAYAL TEJANI, a representative from Indivior, spoke about Perseris. Perseris is an extended release risperidone, indicated for the treatment of schizophrenia in adults. Perseris is available as a 90 or 120 mg once monthly subcutaneous injection. And it should always be administered by a healthcare professional. For patients who have never taken risperidone, oral tolerability should be established prior to initiating Perseris. Based on our clinical evaluations, looking at average

plasma concentrations, 90 mg of Perseris corresponds to 3 mg daily oral risperidone and 120 mg corresponds to 4 mg daily oral risperidone. Patients who were stable on doses other than 3 or 4 mg of oral risperidone may not be candidates for Perseris.

A pivotal phase three double blind randomized placebo-controlled trial of Perseris evaluated the primary endpoint of change in PANSS score and the secondary endpoint as change in CGI-S scores from baseline to the end of study at day 57. The trial included adults with a diagnosis of schizophrenia who were in acute exacerbation prior to screening and would have benefited from a psychiatric hospitalization or continued hospitalization. Eligible patients were randomized to receive two doses of Perseris 90 mg, 120 mg or placebo. A statistically significant improvement was observed in both PANSS and CGI-S scores from baseline to day 57 in both groups receiving Perseris 90 and 120 mg.

The most common adverse reactions seen in clinical trials with Perseris were weight gain, somnolence and musculoskeletal pain. Please refer to the full prescribing information including box warnings for Perseris. Thank you for your time today. And we respectfully request that you consider the designation of Perseris as formulary preferred as an additional option for the treatment of schizophrenia in adults.

MARGARET OLMON, a representative from Abbvie, spoke about cariprazine, brand name Vraylar. Vraylar is a once daily oral medication for adult patients approved for the treatment of schizophrenia, the acute treatment of manic or mixed episodes of bipolar I disorder and the treatment of depressive episodes associated with bipolar I disorder, also known as bipolar depression.

Vraylar has established safety and efficacy in nine separate clinical trials, three trials for schizophrenia, three trials for manic or mixed episodes of bipolar I disorder and three trials for bipolar depression. As such and unlike most atypical antipsychotics, Vraylar treats the full spectrum of bipolar I disorder, manic, mixed and depressive episodes. The most common adverse events of Vraylar included akathisia and extrapyramidal symptoms, though discontinuation due to these side effects was 2% or less in the pivotal studies. Vraylar has a neutral metabolic profile and minimal risk of weight gain, which is a common side effect with other antipsychotics. Vraylar does have most of the same warnings and precautions as other atypical antipsychotics, but I encourage you to review the full prescribing information at rxabbvie.com for complete safety and efficacy information.

While the precise mechanism of action is not fully characterized, Vraylar is unique among the atypical antipsychotics for having the highest affinity for the d3 receptor. Vraylar is the only d3 preferring atypical antipsychotic available, which may have potential benefits on the difficult to treat symptoms of schizophrenia, such as predominant negative symptoms and cognitive defects.

Vraylar has an active metabolite, which contributes to most of the antipsychotic activity with long life estimated to be between one and three weeks. This long half-life suggests that some continued effects may persist after discontinuation of treatment. I believe this should be important to you as it may be beneficial in preventing rapid relapse in patients with intermittent adherence. In a 97 weeks schizophrenia relapse prevention trial, where stable Vraylar patients

were randomized to placebo are allowed to continue on Vraylar, the placebo group maintain prior treatment benefits for over six weeks before increasing rates of relapse were seen.

Dr. Umang Patel 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 afflicts 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. And 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 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.

Next, we have bipolar disorder. Lifelong prevalence estimates bipolar disorder ranging from 0.9% to 2.1%, 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, and these symptoms are outlined here. I put the APA's guidelines in 2002, just for completeness, but we will not be reviewing that.

And next we have Tourette's disorder. The prevalence of Tourette's disorder is unknown. But observational studies have suggested about 1% in school aged children, it is a genetic tic disorder characterized by motor and vocal tics. Generally, individuals have repetitive stereotyped movements of vocalizations such as sniffing, muscle tension, blinking. The criteria for Tourette's disorder states multiple motor and/or one vocal tic are present during the illness and have been present for one year or longer, although they can wax and wane in frequency. Onset of these symptoms must occur prior to 18 years of age to be considered Tourette's. Peak tic severity typically occurs between ages 10 and 12 years of age, and tics usually improve during

adolescence with 18% of those older than 16 years experiencing no tics and 60% having minimal or mild tics six years after initial examination.

Moving on to the next slide here we have Saphris. There was a discontinuation in February 2021, where Allergan made a business decision to discontinue the 5 mg sublingual tablet presentation package in a box of 100. These were 10 blisters with 10 tabs. And the 10 mg sublingual packs in the box of 100, 10 blisters with 10 tablets. All other packaging configurations are still available.

Next we have clozapine. And this is for all its brand partners, we have Clozaril, Versacloz, FazaClo ET. In July, 2021 REMS program updates to remove reference to FazaClo and manufacture Jazz from guide for healthcare practitioners and clozapine REMS website. They added a generic ODT by Teva, to the generic product table on the REMS website. And the FDA has approved the modification to the clozapine REMS program starting November 15, 2021, new requirements will be instituted. Pharmacies will not be able to use the telecommunication switch for verification of safe use conditions. And the patient status form will be used to document monitoring for all outpatients on a monthly basis. Prescribers and pharmacies will be required to recertify by 11/15. And prescribers will be required to re enroll patients who will continue clozapine by this date as well.

In May 2021, the FDA approved Lybalvi, a combo of an atypical antipsychotic and an opioid antagonist indicated for the treatment of schizophrenia in adults and bipolar I disorder in adults for the acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate, as well as for maintenance monotherapy treatment.

In terms of warnings, there is a black-box warning. Elderly patients with dementia related psychosis treated with antipsychotic drugs are at an increased risk of death. Lybalvi is not approved for the treatment of patients with dementia related psychosis. Pregnancy, it may cause EPS and/or withdrawal symptoms in neonates and third trimester exposure. And renal impairment where it is not recommended in patients with end stage renal disease. As you can see, the starting doses are stratified by indication and by specific sub indication of bipolar I disorder. And the availability are found in tablets, ranging from 5 and 10 mg combos all the way up to 20, 10 mg combinations.

Lastly, we have Invega Hafyera, in September 2021, FDA approved an every six-month Invega injection for the treatment of schizophrenia in adults, after they have been adequately treated by Invega Sustenna, which is once monthly or Invega Trinza, which is every three months. It is approved as an injectable suspension in a very specific dose, 1092 mg/3.5 mL and 1560 mg/5 mL single dose syringes. The warnings are very similar. There is a class black-box warning for antipsychotics for elderly patients, it may cause EPS in patients who are pregnant and neonates and it is not recommended in patients with renal impairment. The dose is stratified by patient's previous extended release injectable suspension. So whether they were on Invega Sustenna or Invega Trinza, there is a very specific dosing table that can be found in the PCR or the PI. And as I mentioned earlier, the availability is very specific extended release injectable suspension.

And the last slide for antipsychotics, we have utilization were roughly 95% was in line with PDL. In the previous year's motion, Dr. Phillips moved the drugs in the class were therapeutic alternatives to include at least one oral preparation, one IM injection, two long acting intramuscular injectables, one of which with a duration of at least four weeks. This was seconded by Mr. Riley and passed with one committee member not responding.

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)

Dr. Umang Patel gave the Magellan presentation on antidepressants. For antidepressants prevalence of 12 month and lifetime, MDD is approximately 17.3 million American adults or 7.3% of the population. Women experience depression more often than men. In addition, the prevalence of depression in 2017 was estimated at 3.2 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 two or more treatment attempts of adequate dose and duration of a single depressive episode. In 2019, Spravato 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 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.

Continuing onward with this, during patient evaluation and ongoing follow-up, providers must monitor patients for suicide risk, which should include inquiries regarding suicidal thoughts, plans, intents, means and behaviors. Specific psychiatric symptoms and medical conditions that may impact the likelihood of a suicide attempt, past suicidal ideations and a family history of mental illness, current stressors or protective considerations, and patient support, symptom and independence, among others. The treatment approach in patients with depressive symptoms with acute suicidal ideations or behavior remain similar, but the APA depression guidelines recommend establishing a therapeutic alliance, close surveillance and consideration of an increased intensity of treatment.

Antidepressants are the mainstay of therapy in select cases of acute suicide risk, ECT also, maybe considered. Treatment selection may also be impacted by medication safety in an overdose. Additional agents may be used to augment antidepressants but are not approved for depression such as lithium, mood stabilizers, or the prevention of suicide such as anti-psychotics.

Again, the only approved agent in this class specifically for depressive symptoms of acute suicidal ideation or behavior is Spravato. For approval, its use was studied in combination with initial inpatient hospitalization, and comprehensive standard of care treatment including newly initiated or optimized antidepressants.

Trazodone have carry issued a voluntary recall for one lot of Sildenafil and then one lot of trazodone to the consumer level due to a product mix up resulting in the agents inadvertently packaged together during bottling at a third party facility. To date, no adverse events related to the recall have been reported. In terms of discontinuation, Allergan has announced discontinuation of brand name Sarafem tablets, 10 and 20 mg due to business reasons. And there is a generic version available from point. And in terms of new generics paroxetine hydrochloride, in September 2021, FDA approved a generic for Apotex's Paxil suspension from Novadium. It is the only FDA approved generic product at this time.

In October 2021, the FDA approval for sertraline hydrochloride (Zercapli) as an SSRI for the treatment of MDD in adults and OCD in pediatric patients 6 years of age or older, and it is applied as an oral capsule in the strength of 150 mg. In terms of warnings, there's a class wide black-box warning for increased risk of suicidal thoughts and behavior in pediatric and young patients taking antidepressants. For pregnancy, third trimester use may increase risk of persistent pulmonary hypertension, and symptoms of poor adaptation. And it is not recommended in hepatic impairment. The dosing is 150 mg or 200 mg daily. And the availability is in capsule forms for both of those strengths.

For antidepressants, both the utilization of motions are broken down by SSRIs and others. And so what I will do is I will just do SSRIs first and then the motion and then once that passes, I will go to others. So for SSRIs, roughly 96% are in line with the PDL. The previous year's motion, Dr. Liljegren moved a class effect. And this was seconded by Miss White and passed unanimously.

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

MDD: Others Category (Green Class)

Dr. Umang Patel gave the Magellan presentation on Antidepressants Others. The current utilization is roughly 94% in line with PDL. Dr. Philips moved the drugs in the class were therapeutic alternative last year and seconded by Mr. Riley.

Dr. Liljegren stated that if Spravato is included in this class, she would be kind of disappointed, because she has such mixed feelings about this drug. She points out that there are three transformed studies, and only one met criteria to pull away from placebo. And the difference between the mild risk was only like about four points, so she has questions as to how the study was done.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUDIC ALTERNATIVES, SECONDED BY DR. RYAN. 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)

LINDA FINCH, a representative from Biogen spoke about Aducanumab, which is marketed as Aduhelm. It is indicated for the treatment of Alzheimer's disease. Treatment should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was studied in clinical trials. There are no safety or efficacy data for treatment at earlier or later stages. And this indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in treated patients. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

Titration is required for treatment initiation with a recommended final dosage of 10 mg/kg administered as an IV infusion every four weeks. I wanted to address the proposing length of initial authorization for Aducanumab by Alaska Medicaid, which is three months. And the renewal criteria, which requires documented evidence the patient is responding positively and has failed the rate of cognitive decline. Titration to the recommended dosage of 10 mg/kg takes a minimum of six months, it can take longer if a patient experiences ARIA, which has an adverse event that occurs with removal of amyloid.

In our phase 3 trials, which included a six-month titration, amyloid beta levels in the high dose group did not diverge from levels of a low dose group until patients had greater than six months of treatment. And the primary clinical endpoint in the study, the CDR sum of boxes did not diverge until after 12 months of treatment from placebo. We also have results from an earlier

study which did not use titration except in one arm that showed that amyloid beta reduction was detectable by six months, but clinical effects were not seen until one year. So, patients that were treated with Aducanumab who had decreased amyloid compared to patients who were placebo, after one year of treatment demonstrated a stabilization of clinical decline on the clinical endpoints of CDR sum of boxes in mini mental state exam.

So based on these findings and initial authorization period of at least 12 months will be necessary to evaluate a clinical response to treatment. There are no contraindications for Aducanumab. The warnings and precautions include ARIA-E and ARIA-H which includes micro hemorrhage and superficial siderosis, ARIA-E which is edema and ARIA-H which is hemorrhage were observed in 41% of patients treated with a planned dose of 10 mg/kg compared to 10% of patients on placebo.

And the following AEs were at least 2% higher than placebo in studies one and two. ARIA-E, headache, ARIA-H micro-hemorrhages, ARIA-H superficial siderosis, falls and diarrhea and confusion or altered mental status. So enhanced clinical vigilance is recommended during the first eight doses, and the majority of ARIA was observed in both studies. Although ARIA can occur any time and to monitor for ARIA, brain MRIs within one year of treatment initiation and prior to the 7th and 12th infusions are recommended. So I will refer you, since the amount of time to the additional warnings and precautions on the label.

Dr. Umang Patel gave the Magellan presentation on Dementia: Alzheimer's Agents. Dementia, characterized by irreversible loss or decline in memory and other cognitive abilities affects approximately 5.8 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.

In June 2021, FDA approved Aduhelm, which is an amyloid beta directed antibody indicated for the treatment of Alzheimer's disease. Now, the treatment with Aduhelm should be initiated in patients with mild cognitive impairment or mild dementia stage of disease. The population in which treatment was initiated in the clinical trials. There is no safety or efficacy data on initiating treatment at earlier or later stages of the disease when were studied. This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with Aduhelm.

In terms of limitations, amyloid related imaging abnormalities can occur, enhanced clinical vigilance work for ARIA is recommended during the first eight doses of treatment with Aduhelm, particularly during titration. If a patient experiences symptoms, which could be suggestive of ARIA, clinical evaluation should be performed, including MRI testing.

In terms of dosage, it is the recommended maintenance doses 10 mg/kg administered IV infusion over an hour every four weeks. And there are specific recommendations on when to scan for

MRIs as well. The availability is an injection of 170 mg/1.7 mL solution in single dose vial and 300 mg/3 mL solution in a single dose vial as well. In terms of specialized populations, those studies were conducted to evaluate the PK of this medication in patients with renal and/or hepatic impairment.

On the next slide here, you'll see roughly 95% of the utilization in line with PDL. And the previous year's motion, Mr. Riley moved the drugs in the class were therapeutic alternatives, which was seconded by Dr. Phillips and passed unanimously.

Dr. Carlson discussed that the entire expert channel on the Aduhelm drug discussion voted against it. And it was only the commissioner that approved it. He wanted to know what a group like Alaska Medicaid do when all of the experts on the FDA panel said this is not a drug that should be given at this time.

Dr. Phillips discussed that part B Medicare fees are going to go up over $20 this year just in anticipation of having to pay for a bunch of Aduhelm. She has grave hesitancy about having it on the list until she sees what it does in the real world.

Dr. Carlson agreed that it was hard for him to vote for something where all of the experts on the expert panel said it should not be approved.

DR. LILJEGREN MOVED THAT ADUHELM SHOULD BE EXCLUDED FROM THERAPEUTIC ALTERNATIVES, SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

Break from 10:57 a.m. to 11:07 a.m.

A roll call was taken, and Dr. Riley, Dr. Liljegren, Dr. Carlson, Dr. Doran-Atchison, Dr. Phillps, Dr. Harrison and Dr. Ryan were present.

4-I. NSAIDs

NSAIDs: (Blue Class)

Dr. Umang Patel gave the Magellan presentation on NSAIDS. NSAIDs are commonly used to treat rheumatoid arthritis, osteoarthritis and pain from various ideologies. They are the most widely used drug in US with approximately 80 million prescriptions billed yearly, which accounts for roughly 5% of all prescriptions. It is estimated that OTC NSAIDs are used five to seven times more often than prescription NSAIDs. Most oral NSAIDs are now available as generics and generally considered to be safe and effective. NSAIDs are associated with adverse effects including GI bleeding, PUD, hypertension, edema and renal disease. In addition, NSAIDs have been linked with an increased risk of MIs which is reflected in the box warnings for all NSAIDs. In July 2015, the FDA issued a safety alert, strengthening the existing warning of the increased risk of heart attack and stroke associated with NSAIDs.

The American College of Rheumatology in 2019 stated when pharmacologic treatment is required, the clinical practice guidelines strongly recommend oral NSAIDs for hand, knee, and hip osteoarthritis. Topical NSAIDs are strongly recommended for knee osteoarthritis and conditionally recommended for hand. In 2020, the guidelines on the management of gout strongly recommend oral colchicine, NSAIDs or glucocorticoids as first line treatments for gout flares over other agents and patient factors should determine which agent to use.

Moving onward to ACP and AAFP guidelines in 2020. They published new clinical practice guidelines on the management of acute pain associated from non-low back musculoskeletal injuries in adults who are outpatient. Recommendations are provided for nonpharmacologic and pharmacological treatment modalities. Clinicians are recommended to treat patients with topical NSAIDs with or without menthol gel as first line therapy to decrease or relieve symptoms and to improve physical functioning and the patient's treatment satisfaction.

It is suggested that clinicians treat patients with oral NSAIDs or with oral acetaminophen to reduce pain. Additionally, it is suggested that clinicians treat patients with specific acupressure for reduction of pain and improvement of physical functioning or with transcutaneous electric nerve stimulation. Lastly, it is suggested against clinicians treating patients with opioids including tramadol.

In terms of FDA communications in October 2020, FDA is requiring labeling changes for all prescription and OTC NSAIDs to advise the risk of rare but serious kidney problems in unborn babies that result in low amniotic fluid level. FDA recommends that NSAIDs use be limited between 20 weeks to 30 weeks of pregnancy because of this risk and warnings to avoid NSAIDs after about 30 weeks of pregnancy are already included in the labeling due to the risk of fetal cardiac issues.

In January 2021 for ketorolac, Fresenius Kabi issued a voluntary recall of one lot of ketorolac injection due to presence of particulate matter. No adverse effects were reported to date, but administration of products with the particulate could obstruct blood vessels, potentially leading to clots.

In May 2021, the FDA approved Zipsor which is an NSAID for the relief of mild-to-moderate acute pain in adult patients, 12 years of age or older. Previously, it was only approved in adults, so it is now expanded into the pediatric ages. No updates to any of the limitations, dosage or availability and in terms of specialized population in a commission note, patients with hepatic disease may require dose adjustment for Zipsor compared to patients with normal hepatic function. In terms of utilization, roughly 99.6% of the utilization is in line with PDL. The previous motion, Mr. Riley moved the class effect to go to topical preparation, which was seconded by Dr. Phillips and passed unanimously.

DR. CARLSON 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)

Dr. Umang Patel 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% 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 '99 to 2015, and during 2015 alone, 33,000 people in the US have died from opioid-related overdoses. The overdoses were higher among men being about 14% compared to females, which was 7%.

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. In terms of the ACP and AAFP guidelines, I just reviewed this in the NSAIDs, so I will not be going through this, but since this was pain related, I wanted to put this in here as well.

The first medication we have here is morphine sulfate tablets and morphine sulfate's oral solution. So in June 2021, 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 adults. Additionally in June 2021, they also approved an expanded indication for morphine sulfate oral solution 2 mg/mL and 4 mg/mL in pediatric patients 2 years of age or older with acute pain severe enough to require an opioid analgesic, for which alternative treatments are inadequate, previously only indicated for adults. No changes in the warnings, dosage or availability as well.

In terms of patients who are of reproductive potential, prolonged use of morphine sulfate tablets during pregnancy can result in neonatal opioid withdrawal symptoms, which may be life threatening if not recognized and treated. So, it is noteworthy to show that it can have fetal risk in pregnant patients as well.

On the final slide here, in terms of FDA communications in February 2021, FDA issued a warning letter to AceIRx regarding false and misleading claims about the product DSUVIA and its risks and benefits.

On the next and final slide for this about 46% was in line with PDL. Previous year's motion, Dr. Phillips moved the drugs in the class were therapeutic alternatives, which was seconded by Mr. Riley and passed unanimously.

Dr. Phillips asked if the skew was towards non-PDL due to generics, and Dr. Patel 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. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, SECONDED BY DR. CARLSON. THE MOTION PASSED UNAIMOUSLY.

Long-Acting Opioids: (Green Class)

Dr. Umang Patel gave the Magellan presentation on Long-Acting Opioids.

In September 2020, the FDA issued warning letters to 17 website owners worthy of illegal sales of unapproved and misbranded opioids. This includes those sold without a prescription and products without adequate directions for use. And in January 2021, the FDA released an update on the steps being taken to address the opioid crisis, particularly in regards to the REMS program. Other efforts include reducing unnecessary exposure to prescription opioids and preventing new addiction, support for treating opioid use disorder, assisting in development of new pain treatments and addressing contributors to the illegal importation/sale of opioids. Regarding the REMS Program, the FDA is strengthening the program for transmucosal immediate release fentanyl (TIRF) products to ensure the benefits continue to outweigh the risk by finalizing modifications to the REMS Program. Efforts are also underway to assess the opioid analgesics.

Roughly 58% was in line with PDL. Previous year's motion, Dr. Phillips moved the drugs in the class of therapeutic alternatives to include at least one oral preparation, one transdermal and at least one abuse deterrent preparation. This was seconded by Ms. White and the motion passed unanimously.

Dr. Liljegren wanted to know why so many were on the mandatory non-PDL, Dr. Patel clarified that Primary contributors were OxyContin and methadone.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS OF THERAPEUTIC ALTERNATIVES, DR. CARLSON SECONDED THAT MOTION. THE MOTION PASSED UNANIMOUSLY.

4-K. Neuropathic Pain

Neuropathic Pain: (Green Class)

Dr. Umang Patel gave the Magellan presentation on Neuropathic Pain. In terms of neuropathic pain, it can be caused by several different diseases such as diabetes, herpes zoster, HIV or even medical interventions. It has recently been defined as a pain that evolves as a result of direct injury or disease to the nervous system, specifically the somatosensory. Fibromyalgia is a chronic disorder characterized by pain, fatigue and sleep disturbances, predominantly affects women and is difficult to treat and a multidisciplinary approach should be utilized. For the newer medications in this class, again please note all guidelines for this class are over a year old and they are in the appendix. So, we will move right along to clinical updates.

Drizalma Sprinkle was a medication in which July 2021, FDA approved new indication of fibromyalgia in adults. Previously, it was only indicated for the following in adults: MDD, generalized anxiety disorder, diabetic peripheral neuropathic pain and chronic musculoskeletal pain as well as GAD in pediatric patients 7 years to 17 years of age. No changes to any of the warnings or availability, so has a black box warning in hepatotoxicity. The dosing for this new indication is starting dose of 30 mg per day with a targeted maximum dose of 60 mg per day. And lastly, there was a new generic in April 2021, FDA approved multiple generic for Pfizer's Lyrica CR; from Alvogen, Apotex, MSN, Mylan and Sun.

Pretty quick class here, in terms of utilization, roughly 99% in line with the PDL. Previous year's motion, Dr. Phillips moved the drugs in the class of therapeutic alternatives, seconded by Mr. Riley and it passed unanimously.

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

4-L. Anti-Migraine Agents

Anti-Migraine Agents: (Blue Class)

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

RYAN NORMAN, a representative from Teva Pharmaceuticals Field Value Evidence and Outcomes team in the US Medical Affairs Division, provided some updated information about Ajovy, also known as fremanezumab.

So as a top cause of disability in United States, migraine is a complex and widespread neurological disease. It impacts nearly one in four US households. And the struggle with adherence and persistence to non-migraine specific preventive treatments is low and it tends to decline overtime. According to one study that was assessing adherence to 14 commonly prescribed oral migraine-preventive medications and this was among patients with chronic migraine, adherence was generally low to all oral migraine preventive medications with about 26% adherence at six months and then only about 17% at 12 months. In addition to the adherence and persistence problems, higher healthcare resource utilization costs are observed

among the subgroups of patients with preventive migraine medications that often switch or discontinue the medicine. So looking at Ajovy's real world evidence and evaluating Ajovy, comparing before and after Ajovy initiation, the following was found statistically significant. When looking at an analysis of pharmacy claims, the total number of acute medications, specifically opioids and triptans as well as the proportion of patients filing claims for these medications was overall lower.

There was a separate analysis done on EMR and claims records regarding migraine intensity and pain and migraine intensity of pain among this population was also significantly decreased. Ajovy does have a favorable flexible dosing option for adherence with whether it is a quarterly dosing, so once every three months, or a monthly dosing available.

Switching quickly to Ajovy's clinical development program, across 24 clinical studies, over 4000 patients that had migraine were exposed to Ajovy. And during this time, no additional safety signals were seen across the exposed population. And with the pool data from the phase-3 trials that indicated treatment with Ajovy for 12 weeks also had a cardiovascular safety profile similar to placebo. Currently, the safety and efficacy of fremanezumab is being evaluated and investigated in fibromyalgia, which is in a phase-2 randomized controlled clinical trial as well as additional phase-4 trials with fremanezumab being studied in preventive treatment of migraine patients with major depressive disorder [Inaudible: 22:57] migraine and migraine in children and adolescents.

MARGARET OLMON, a representative from AbbVie, spoke about Ubrelvy and the new medication, Qulipta for the patients who suffer with migraine headaches. The American Headache Society states that acute migraine treatment should restore the patient's ability to function free from headache pain with minimal adverse events. The goals in migraine prevention are to reduce headache frequency, severity and duration as well as to reduce the use of acute medications, reduce disability and improve quality of life.

For those individuals with fewer than four migraine headaches per month, acute rescue treatment with Ubrelvy will help to lessen the pain and reduce their bothersome symptoms that allow the patients to get back to their day. Providers and patients have also needed a preventive oral option with high effectiveness and one that is well tolerated. Today, I would like to focus on this new option for them, Qulipta, also called atogepant, which is an oral CGRP receptor antagonist developed specifically for preventing migraines. A phase-3 study of atogepant in the advanced trial evaluated the oral daily doses of 10, 30 and 60 mg in 902 patients with 4 to 14 monthly migraine days. The primary efficacy endpoint was changed from baseline and mean monthly migraine days across the 12 weeks of the trial. The patients on Qulipta achieved a clinically and statistically significant reduction in about 4 migraine days per month. Fewer patients experienced a migraine day versus placebo as early as day 1 after their first dose. Atogepant also significantly reduced their mean monthly acute medication days by approximately 50%.

Looking at migraine days in weeks 9 through 12 of the study versus migraine days at baseline, 60% to 70% of patients experienced a 50% reduction and 1 in 4 patients had no migraines the final four weeks of the trial. Adverse events were mostly mild to moderate and included constipation, nausea, and upper respiratory tract infection. Discontinuation rates were below 1%

and were not dose related. Qulipta also offers quick clearance if needed for abrupt discontinuation of therapy. Along with Ubrelvy, patient's providers also have Qulipta as an effective and well-tolerated preventive medication that significantly reduces migraine days, acute medication use and the disability associated with episodic migraine. I would like to respectfully request that both Ubrelvy and Qulipta be preferred medications for the patients of Alaska. Thanks for your time and consideration, and I would be happy to answer any questions you might have.

Dr. Umang Patel 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 39 million men, women and children in US. It is one of the most common complaint 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, 18% of women, 6% of men and 10% of children 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. 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.

Next, we have Nurtec ODT. In June 2021, FDA approved new indication for the preventative treatment of episodic migraines in adults that was already indicated for the acute treatment of migraines with or without aura in adults and no changes to warnings. There is a new dosage for this new indication, where it is 75 mg taken orally every other day and the maximum is 75 mg in a 24-hour period and no changes to availability here as well.

On the next slide here, in June 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. And lastly, MI and/or infarctions, other cardiac adverse reactions [Inaudible: 30:55] as well.

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. And again, this is 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.

On the next slide for utilization is similar to the antidepressants, but there are two subclasses and two motions. So, I will go through the first one first. For triptans, approximately 96% was in line with the PDL. Previous year's motion, Dr. Liljegren moved that triptans can be considered a class effect to include at least one non-oral preparation, and this was seconded by Mr. Riley and passed unanimously.

DR. LILJEGREN 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. DORAN-ATCHISON SECONDED THAT. THE MOTION PASSED UNANIMOUSLY.

4-M. Skeletal Muscle Relaxants

Skeletal Muscle Relaxants: (Green Class)

Dr. Umang Patel gave the Magellan presentation on Skeletal Muscle Relaxants. The utilization where roughly 98% is in line with PDL. Previous year's motion, Dr. Liljegren moved the drugs in the class were therapeutic alternatives, excluding carisoprodol from the PDL seconded by Ms. White and passed unanimously.

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

4-N. Restless Legs Syndrome

Restless Legs Syndrome: (Green Class)

Dr. Umang Patel gave the Magellan presentation on Restless Legs Syndrome. And for restless leg syndrome, we have, so utilization, none are in line with PDL. Dr. Liljegren moved the class effect previously, seconded by Dr. Phillips and passed unanimously. Keep in mind the, when it says not in line with PDL, that includes medications that are nonpreferred, which was Nupro, which is one medication, and then there were two others that were non-reviewed and so that is why it is saying not in line with PDL.

Dr. Riley recalled that it was voted class effect a year ago. So, were the two that are non reviewed.

Dr. Ryan believed that last year they were broken off from the anti-Parkinson's agents just to the RLS only, which is why he probably changed that NR, but he is pretty sure those two generics are preferred. So, literally 99% is going to be on the PDL.

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

4-O. Smoking Cessation

Smoking Cessation: (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Smoking Cessation.

He stated that the US Preventive Services Task Force in 2020 issued a recommendation for school-aged children and adolescents who have not started to use tobacco stating that primary care clinicians are recommended to provide intervention such as education or group counseling in order to prevent tobacco use initiation in these individuals. However, for school-aged children and adolescents who use tobacco, it was concluded that current evidence was inadequate to determine the benefits versus risks of primary care-feasible interventions regarding tobacco cessation.

The American Thoracic Society last year published new clinical guidelines on initiation of pharmacotherapy for tobacco dependence. The guidance maintains all patients who are using tobacco should receive treatment for dependence and not only be encouraged to discontinue tobacco use. Strong recommendations include preference for use of varenicline over nicotine patch, preference over bupropion, use of varenicline rather than a nicotine patch in adults with comorbid psychiatric conditions, starting in adults even if they are not ready to quit and using controller therapy for an extended duration of more than 12 weeks. Conditional recommendations include the combination of a nicotine patch with Chantix over use of Chantix alone and use of Chantix over electronic cigarettes.

This year in 2021, the US Preventive Services Task Force recommended that clinicians ask all adults about tobacco use and to advise users to stop using tobacco and provide behavioral interventions, including pharmacotherapy for tobacco use cessation. Clinicians should also advise pregnant women to stop using tobacco and provide behavioral interventions. However,

evidence is not sufficient to assess benefits versus risk. In April 2020, I apologize, these last two bullets were already stated previously, I put these in here just as a summary for 2021 so they were reaffirmed.

On the next slide for drug recalls, first one being Chantix in July 2021, Pfizer expanded its voluntary recall due to the presence of carcinogen N-nitroso-varenicline above the company's acceptable limits of -- for this impurity to 12 lots at the consumer level. The FDA advises patients taking recalled varenicline to continue taking their current medicine until their pharmacist provides a replacement or their doctor prescribes an alternative. Since your patient access, the FDA will not object to certain manufacturers temporarily distributing the tablets above FDA's acceptable intake limit of 37 nanograms per day but below the interim acceptable intake limit of 185 nanograms per day until the impurity can be eliminated or reduced to acceptable levels. And the agency continues to evaluate data and may update the interim acceptable limits in the future. There was also a new generic, FDA reported the first approval of the first generic of Pfizer's Chantix, Chantix 0.5 and 1 mg tablet from Par. And Par has launched its generic varenicline as well.

In terms of utilization, roughly 97% was in line with the PDL. Previous motion, Dr. Phillips moved the drugs in the class were therapeutic alternatives, which was seconded by Mr. Riley and passed unanimously.

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

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

Opioid Dependence: (Green Class)

DESIREE CREVECOEUR-MACPHAIL, a representative from ICMA Community Health, presented information on Kloxxado, an 8 mg naloxone hydrochloride nasal spray. Kloxxado is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose as manifested by respiratory and/or central nervous system depression in adult and pediatric patients. There is an unmet need for a higher dose of naloxone. Opioid overdose deaths have increased from 2019 to 2020 in Alaska and other states. Across the country, deaths attributed to other synthetic opioids like illicitly manufactured fentanyl exceed those caused by other opioids including heroin and commonly prescribed opioids.

In addition, in 2018, about half of the cocaine-involved deaths and about a quarter of the stimulant-involved deaths also involved synthetic opioids. The adulteration of other drugs with illicitly manufactured fentanyl implies a need for a higher-dose naloxone. They are more potent and faster acting than other opioids. Overdoses involving illicitly manufactured fentanyl often require multiple doses of naloxone. For example, the need for a higher-dose naloxone is reflected in real world using naloxone by both bystanders and emergency services. Data examining naloxone administration show increases in the number of opioid overdose events were two more doses of the 4 mg naloxone nasal spray was used from 34% in 2016 in one study to as

high as 78% in a 2021 study, we're preparing for publication. EMS data shows an increase of 96% over eight years in the number of opioid overdose events, where two or more doses of naloxone were used. This suggests that in many cases, a single dose of naloxone may be insufficient to reverse the respiratory depression that results from an opioid overdose.

Furthermore, Dr. Patrice Harris, head of the AMA Opioid Task Force stated that the FDA is making sure the overdose reversing drug is potent enough to counteract the increasingly lethal and illicitly manufactured fentanyl. Kloxxado is an 8 mg naloxone hydrochloride nasal spray. It contains twice as much naloxone per spray as the current intranasal naloxone medication. Naloxone is a safe medication that has been used to address opioid overdoses for 50 years.

Kloxxado again is indicated for the emergency treatment of known or suspected opioid overdose as manifested by respiratory and/or central nervous system depression and is safe for adult and pediatric patients. It is not a substitute for emergency care, but it is intended for immediate administration as emergency therapy where opioids may be present. It is contraindicated for anyone with hypersensitivity to naloxone hydrochloride or any of the other ingredients in Kloxxado.

There are three warnings for Kloxxado which are indicated in the package insert, risk of recurrent respiratory nervous system depression, limited efficacy with partial agonist mixed agonist-antagonist or if you administer Kloxxado to someone whose opioid dependent, there is a risk of precipitated withdrawal.

Dr. Umang Patel gave the Magellan presentation on Opioid Dependence. He stated that utilization where roughly 95% is in line with the PDL. Mr. Riley moved the drugs in the class were therapeutic alternative to include at least one long-acting injectable product. This was seconded by Dr. Liljegren and then passed unanimously.

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

Reversal Agents: (Blue Class)

Dr. Umang Patel gave the Magellan presentation on Reversal Agents. There is an estimated 36 million Americans aged 12 years and older who were current in the past month illicit drug users. There were approximately 1.6 million people aged 12 years or older in the US who misused opioids in the past year, approximately 20 million aged 12 years or older in 2018 were considered to have a substance use disorder including 15 million with an alcohol use disorder, 8 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 April 2021, FDA approved a new higher-dose naloxone hydrochloride nasal spray that delivers 8 mg naloxone to treat opioid overdose, previously approved as 2 mg and 4 mg naloxone nasal spray products. Again, since this was a higher dose of an existing medication, no changes to indications, warnings or dosage. Just again it is a 8 mg in 0.1 milliliter naloxone nasal spray.

Moving onward to the utilization 100% in line with PDL. Previous year's motion, Dr. Liljegren moved the drugs into class-4 therapeutic alternatives to include Narcan. This was seconded by Dr. Carlson and passed unanimously.

Dr. Liljegren commented that she was thinking that there should be therapeutic alternatives to include Narcan at all available doses or at 2, 4 and 8 mg doses. If anybody have anything to say

Dr. Patel stated that it did come to his attention too. He was wondering kind of what the reason there was only Narcan there as far as, you know, an overdose treatment, and I guess some of the other injectables are no longer being made, so that is why it is Narcan.

DR. LILJEGREN MOTIONED THAT THE DRUGS IN THE CLASS ARE THERAPEUTIC ALTERNATIVES TO INCLUDE NALOXONE IN ALL DOSES AVAILABLE. DR. CARLSON SECOND THAT MOTION. THE MOTION WAS PASSED UNANIMOUSLY.

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

Charles Ryan gave the Magellan presentation on RSV Monoclonal Antibodies. He stated that this year with COVID, there was kind of a surge in RSV cases. The program did open up Synagis to members. He believes that right at the very beginning of September and our October utilization is pretty much on par with what I would expect for a normal season. And the RSV Committee made up of healthcare providers from all over the state is going to meet on Monday to update the criteria as we enter the normal season.

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

4. Review Minutes from September 2021

There were no changes to the meeting minutes of April 2021.

DR. RILEY MOVED TO APPROVE THE MEETING MINUTES OF SEPTEMBER 2021. SECONDED BY DR. CARLSON. THE MOTION WAS PASSED BY ALL MEMBERS WITH THE EXCEPTION OF DR. LILJEGREN, WHO WAS NOT PRESENT AT THE MEETING.

4. End of Public Meeting
5. Comments From Committee Members
6. Adjourn

MR. RILEY MOVED TO ADJOURN THE MEETING. THE NEXT MEETING WAS SCHEDULE FOR JANUARY 21, 2022. WITHOUT OBJECTION, THE MEETING WAS ADJOURNED.