MaineCare Services
An Office of the Department of Health and Human Services
Paul R. LePage, Governor
Ricker Hamilton, Commissioner

Department of Health and Human Services
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TO: Maine Drug Utilization Review Board
DATE: 6/14/2018
RE: Maine DUR Board **Meeting** minutes from June 12, 2018

ATTENDANCE	PRESENT	ABSENT	EXCUSED
Linda Glass, MD	X		
Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR	X		
Mike Antoniello, MD		X	
Kathleen Polonchek, MD	X		
Kenneth McCall, PharmD		X	
Steve Diaz, MD	X		
Erin Ackley, PharmD.	X		
Corinn Martineau, PharmD.	X		
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare	X		
Jeffery Barkin, MD, Change Healthcare	X		
Christopher Pezzullo, State Health Officer DHHS, DO		X	
Jill Kingsbury, MaineCare Pharmacy Director	X		

Guests of the Board: Ed Bosshart, PharmD, Tom Leet

CALL TO ORDER: 5:30PM

Jill Kingsbury called the meeting to order at 5:30 PM.

PUBLIC COMMENTS

Stefanie Diloreto: Highlighted the attributes of Symdeko.
David Rousso from Spark Therapeutics: Highlighted the attributes of Dyanavel XR.
Amy Tomasello from Tris Pharma: Highlighted the attributes of Lonhala Magnair.
Noel Melter from Vertex: Highlighted the attributes on Symdeko.
Karen Phillips from Amgen: Highlighted the attributes of Aimovig.

OLD BUSINESS

DUR MINUTES

The April DUR meeting minutes were accepted as written.

MAINECARE UPDATE

No update at this time.

NEW BUSINESS

INTRODUCTION: USE OF NALOXONE INTOLERANCE

The opioid epidemic has resulted in a dramatic increase in the utilization of abuse deterrent medications, the most common being the agonist/antagonist combination of buprenorphine and naloxone. While historically buprenorphine alone has been recommended for pregnant patients due to concerns of naloxone exposure in pregnancy, there is little evidence to support buprenorphine use as monotherapy in the non-pregnant patient, due to concerns of abuse and diversion. While there is concern that naloxone can result in seizures, pulmonary edema and cardiovascular effects such as hypotension, hypertension, arrhythmias and sudden death, there is little information about the incidence of these adverse effects, many of which may be seen due to opioid intoxication without naloxone. In general, naloxone is thought to be quite safe.

Change Healthcare will identify non-pregnant members between the ages of 18-75 with a diagnosis of opioid abuse who are prescribed buprenorphine alone for at least 30 days and determine how many of them within the 90 days prior to their first buprenorphine prescription were given a prescription of one of the buprenorphine/naloxone combinations. Through information garnered in the PA process, we can identify the reasons for discontinuing naloxone. We will also identify how many members have been on buprenorphine for 12 months or more.

Board Decision: No action needed at this time.

DATA PRESENTATION: USE OF STATINS IN ASCVD

Statin use has become widespread with the identification of the effect of cholesterol levels on risk of coronary vascular disease. Purported benefits of statins include: anti-atherogenic and plaque stabilizing properties, anti-inflammatory effects, modulation of the autonomic nervous system and anti-arrhythmic properties. Possible deleterious effects include the decrease in lipoproteins, which may help to clear bacterial endotoxins and the lowering of ubiquinone (CoEnzyme Q10).

Recommendation for statin use includes all patients with known ASCVD for secondary prevention. High dose statin therapy is recommended for most patients with LDL-C greater than 70mg/dl, although the value of high dose statins as compared with moderate dose in those over 75 years of age is unclear. It is known that statins are poorly tolerated by many and compliance is an issue. Patients should generally be prescribed the highest dose of statin tolerable, even if below guidelines.

Identify members between the ages of 40-75 with diagnoses of ASCVD and either DM, chronic kidney disease or hypercholesterolemia to see how many have been prescribed at least one statin medication

for secondary prevention within the 2-year time frame. Of those prescribed at least one statin, we will look to see how many remained on a statin medication throughout the duration of the time frame we are investigating. We will stratify the data by age cohort (40-49, 50-59, 60-69, 70-75) and additionally will stratify by the intensity level of the statin prescribed to assess compliance with guidelines.

There were young members on low intensity statins and elderly members on high intensity statins. It is possible that some of those on lower intensity statins were intolerant of higher doses, but we did not examine that in the data.

Nearly half of the members started on a statin with ASCVD and other at-risk diagnoses were on the statin for less than one year, and the intensity of the statin dose was sometimes not in accordance with guidelines. A communication to the broad medical community of primary care providers seems appropriate, reminding them of guidelines for statin use.

Board Decision: The Board unanimously approved the above recommendation.

UPDATED SUBOXONE PA FORM

Change Healthcare presented the board with an updated Suboxone PA form to replace the Suboxone Restart and Continuation PA forms.

Board Decision: No action needed.

THERAPUTIC DRUG CLASS REVIEW PHOSHATE BINDERS NON-CALCIUM

After review of the category it is recommended to move Renvela and Fosrenol to preferred.

Board Decision: The Board unanimously approved the above recommendation

NEW DRUG REVIEW

Aimovug® (erenumab-aooe); **PDL category**- Migraine- Misc.

Erenumab-aooe, the active ingredient of Aimovig®, is a human immunoglobulin G2 (IgG2) monoclonal antibody that has high affinity binding to the calcitonin gene-related peptide (CGRP) receptor. It is produced using recombinant DNA technology in Chinese hamster ovary (CHO) cells. Erenumab-aooe antagonizes CGRP receptor function. It is indicated for the preventive treatment of migraine in adults. The safety and efficacy of Aimovig® were assessed as a preventive treatment of episodic or chronic migraine in 3 randomized, double-blind, placebo-controlled studies. It is the first FDA-approved preventative treatment for migraine in a new class of drugs that antagonizes the activity of calcitonin gene-related peptide. Aimovig® was observed to have statistically significant improvements for key efficacy endpoints as compared with placebo, including monthly migraine days (MMD), MMD responders, and monthly acute migraine-specific medication days. Comparator studies with active ingredients were not found.

Recommendation: Admelog ® be non-preferred.

Clinical Criteria: Aimovig will be available for chronic migraine defined as 15 or more headaches a month. Adequate trial of three preventative treatment medications of 60 days each.

Board Decision: The Board unanimously approved the above recommendation.

Carospir® (spironolactone); **PDL category**- Diuretics

Spironolactone, the active ingredient of Carospir®, and its active metabolites are specific antagonists of aldosterone, acting mainly through competitive binding of receptors at the aldosterone-dependent sodium-potassium exchange site in the distal convoluted renal tubule. Spironolactone causes increased amounts of sodium and water to be excreted, while potassium is retained. Spironolactone acts both as a diuretic and as an antihypertensive drug by this mechanism. It is indicated for the management of Heart Failure- For the treatment of New York Heart Association (NYHA) Class III-IV heart failure and reduced ejection fraction to increase survival, manage edema, and to reduce the need for hospitalization for heart failure (usually administered in conjunction with other heart failure therapies). Hypertension- As an add-on therapy for the treatment of hypertension, to lower blood pressure in adults who are not adequately controlled on other agents. And Edema caused by Cirrhosis- For the management of edema in adult cirrhotic patients when edema is not responsive to fluid and sodium restriction. There is no evidence at this time to support that Carospir® is safer or more effective than the currently available, more cost-effective medications.

Recommendation: Carospir ® be non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Cimduo® (lamivudine & tenofovir disoproxil fumarate**); PDL category-** Antiretrovirals

Cimduo® is a fixed-dose combination tablet for oral administration that contains 2 agents with antiviral activity against human immunodeficiency virus type 1 (HIV-1), including lamivudine (also known as 3TC, a synthetic nucleoside analogue and mainly inhibits HIV-1 reverse transcriptase) and tenofovir disoproxil fumarate (TDF, a prodrug of tenofovir that inhibits the activity of HIV-1 reverse transcriptase). It is indicated to be used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adult and pediatric patients weighing at least 35kg. Cimduo® has a box warning regarding the increased risk of post treatment acute exacerbations of hepatitis B. Severe acute exacerbations of hepatitis B have been reported in those co-infected with hepatitis B virus and HIV-1 and have discontinued lamivudine or tenofovir disoproxil fumarate. Monitor hepatic function and if appropriate, start anti-hepatitis B treatment. While specific studies were not performed with Cimduo, the combination of EFV plus 3TC plus TDF was found to be as effective as the combination of EFV plus 3TC plus d4T through week 48 and week 144 of treatment regarding the percentage of responders (subjects who achieved and maintained confirmed HIV-1 RNA <400 copies/ml).

Recommendation: Cimduo® be preferred

Clinical Criteria: Defer until after Symfi, Symfi Lo and Trogarzo review.

Board Decision: The Board unanimously approved the above recommendation.

Symfi® (efavirenz, lamivudine, & tenofovir disoproxil fumarate); **PDL category**- Antiretrovirals

Symfi® is a fixed-dose combination tablet for oral administration that contains 3 agents with antiviral activity against human immunodeficiency virus type 1 (HIV-1), including efavirenz (EFV, a non-nucleoside, reverse transcriptase inhibitor, or NNRTI), lamivudine (also known as 3TC, a synthetic nucleoside analogue and mainly inhibits HIV-1 reverse transcriptase) and tenofovir disoproxil fumarate (TDF, a prodrug of tenofovir that inhibits the activity of HIV-1 reverse transcriptase). It is indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 40kg. There is limited information on the potential for interactions between efavirenz and drugs that prolong the QTc interval. QTc prolongation has been seen with the use of efavirenz. It is recommended to consider alternatives to efavirenz when co-administered with a drug with a known risk of Torsade de Pointes. Symfi® is a triple-drug regimen indicated as a complete regimen for the treatment of HIV-1 infection in adult and pediatric patients weighing at least 40kg. It should not be administered with other antiretroviral medications for the treatment of HIV-1 infection as it is a complete regimen. The combination of EFV plus 3TC plus TDF was found to be as effective as the combination of EFV plus 3TC plus d4T through week 48 and week 144 of treatment regarding the percentage of responders (subjects who achieved and maintained confirmed HIV-1 RNA <400 copies/ml). Symfi® is the same product as Symfi® Lo except Symfi® has a higher strength of efavirenz (600mg) as compared with Symfi Lo (efavirenz 400mg).

Recommendation: Symfi® be preferred.

Clinical Criteria: Defer until after Symfi Lo and Trogarzo review.

Board Decision: The Board unanimously approved the above recommendation.

Symfi Lo® (efavirenz, lamivudine, & tenofovir disoproxil fumarate); **PDL category**- Antiretrovirals

Symfi® Lo is a fixed-dose combination tablet for oral administration that contains 3 agents with antiviral activity against human immunodeficiency virus type 1 (HIV-1), including efavirenz (EFV, a non-nucleoside, reverse transcriptase inhibitor, or NNRTI), lamivudine (also known as 3TC, a synthetic nucleoside analogue and mainly inhibits HIV-1 reverse transcriptase) and tenofovir disoproxil fumarate (TDF, a prodrug of tenofovir that inhibits the activity of HIV-1 reverse transcriptase). It is used as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 35kg. It should not be administered with other antiretroviral medications for the treatment of HIV-1 infection as it is a complete regimen. The combination of EFV plus 3TC plus TDF was found to be as effective as the combination of EFV plus 3TC plus d4T through week 48 and week 144 of treatment regarding the percentage of responders (subjects who achieved and maintained confirmed HIV-1 RNA <400 copies/ml). In the ENCORE1 study, EFV 400mg plus FTC plus TDF was found to be as effective as EFV 600mg plus FTC plus TDF.

Recommendation: Symfi Lo ® be preferred.

Clinical Criteria: Defer until after Trogarzo review.

Board Decision: The Board unanimously approved the above recommendation.

Trogarzo® (ibalizumab-uiyk); **PDL category**- Antiretrovirals

Ibalizumab-uiyk, the active ingredient of Trogarzo®, is a CD-4 directed post-attachment HIV-1 inhibitor. It is a CD4 domain 2-directed humanized monoclonal antibody of immunoglobulin G (IgG) isotype 4 produced by recombinant DNA technology. Ibalizumab-uiyk is an antiretroviral drug that blocks HIV-1 from infecting CD4+ T cells by binding to domain 2 of CD4 and interfering with post-attachment steps needed for the entry of HIV-1 virus particles into host cells and preventing the viral transmission that occurs via cell-cell fusion. The binding specificity of Ibalizumab-uiyk to domain 2 of CD4 allows Ibalizumab-uiyk to block viral entry into host cells without causing immunosuppression. It is indicated to use in combination with other antiretroviral(s) for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen. In a single-arm study, 83% of subjects receiving Trogarzo® achieved a 0.5 log10 decrease in viral load at the end of the functional monotherapy period.

Recommendation: Trogarzo ® be non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

As part of the review of this category it was recommended that Prezcobix be moved to preferred.

Board Decision: The Board unanimously approved the above recommendation.

Crysvita® (burosumab twza); **PDL category**- AFibroblast Growth Factor 23 Inhibitors

Aprepitant, the active ingredient of Cinvanti®, is a substance P/neurokinin 1 (NK1) receptor antagonist, an anti-emetic agent. In animals, it has been shown to inhibit emesis induced by cytotoxic chemotherapeutic agents, such as cisplatin, via central actions. Animal and human studies have demonstrated that aprepitant augments the anti-emetic activity of the 5-HT3 receptor antagonist ondansetron and the corticosteroid dexamethasone and inhibits both the acute and delayed phases of cisplatin-induced emesis. It was indicated in combination with other anti-emetic agents, is indicated in adults for the prevention of: acute and delayed nausea and vomiting with initial and repeat course of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin AND nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). Cinvanti® has not been studied for the treatment of established nausea and vomiting. The safety and efficacy of Cinvanti® were established based on adequate and well-controlled adult studies of a single-dose of IV fosaprepitant, a pro-drug of aprepitant, and a 3-day regimen of oral aprepitant in chemotherapy-induced nausea and vomiting associated with HEC and MEC, respectively.

Recommendation: Cinvanti ® be non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior

Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Daxbia® (cephalexin); PDL category- Cephalosporins

Daxbia® is a semi-synthetic cephalosporin antibacterial drug. It is a bactericidal agent that acts by the inhibition of bacterial cell-wall synthesis. It is indicated for the treatment of respiratory tract infections- caused by susceptible isolates of Streptococcus pneumonia and Streptococcus pyogenes. Otitis Media- caused by susceptible isolates of Streptococcus pneumonia, Haemophilus influenzae, Staphylococcus aureus, Streptococcus pyogenes, and Moraxella catarrhalis. Skin and Skin Structure Infections- caused by susceptible isolates of Staphylococcus aureus and Streptococcus pyogenes. Bone Infections- caused by susceptible isolates of Staphylococcus aureus and Proteus mirabilis. Genitourinary Tract Infections, including Acute Prostatitis- caused by susceptible isolates of Escherichia coli, Proteus mirabilis, and Klebsiella pneumoniae. It is recommended to monitor and adjust metformin dose if use concomitantly with cephalexin. Concomitant use with probenecid is not recommended. There were no clinical studies found in the prescribing information for Daxbia®; however, cephalexin has been available in other various dosage forms and strengths for numerous years and have proven to be safe and effective. Methicillin-resistant staphylococci and most isolates of enterococci are resistant to cephalexin. Cephalexin is not active against most isolates of *Enterobacter spp*., *Morganella morganii*, and *Proteus vulgaris*. In addition, cephalexin has no activity against *Pseudomonas spp*., or *Acinetobacter calcoaceticus*.

Recommendation: Daxbia®, Cephalexin® Tabs and Cephalexin® 750mg Caps be non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Erleada® (apalutamide); **PDL category**- Cancer

Apalutamide, the active ingredient of Erleada®, is an androgen receptor inhibitor that binds directly to the ligand-binding domain of the androgen receptor. Apalutamide inhibits androgen receptor nuclear translocation, inhibits DNA binding, and impedes androgen receptor-mediated transcription. In animal models of prostate cancer, apalutamide caused decreased tumor cell proliferation and increased apoptosis, leading to decreased tumor volume. It is indicated for the treatment of patients with non-metastatic, castration-resistant prostate cancer (NM-CRPC). A multicenter, randomized, double-blind, placebo-controlled study assessed the safety and efficacy of Erleada® in patients (N=1207) with NM-CRPC. Compared to placebo, Erleada® significantly prolonged metastasis-free survival, time to metastasis, and progression-free survival.

Recommendation: Erleada ® be non-preferred and Xtandi will be preferred.

Clinical Criteria: Erleada will be considered for patients with non-metastatic, castration-resistant prostate cancer (NM-CRPC). DDI: Concomitant use of Erleada® with medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or assess for loss of activity if the medication is continued. Use caution if substrates of UDP-glucuronosyl transferase (UGT) must be co-administered with Erleada® and assess for loss of activity.

Board Decision: The Board unanimously approved the above recommendation.

Gocovri® (amantadine); **PDL category**- Parkinson Disease- Dopaminergics/Carbidopa/Levodopa

Amantadine, the active ingredient of Gocovri®, is a weak uncompetitive antagonist of the NMDA receptor. Amantadine may have direct and indirect effects on dopamine neurons. The exact mechanism by which it works in the treatment of dyskinesia is not known. It is indicated for the treatment of dyskinesia in patients with Parkinson's disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications. The safety and efficacy of Gocovri® for the treatment of dyskinesia with Parkinson's disease were assessed in 2 randomized, double-blind, placebo-controlled studies that included adults with at least 1 hour of troublesome dyskinesia time during the day and at least mild functional impact due to dyskinesia. In clinical trials compared to placebo, Gocovri® significantly reduced dyskinesia burden, as well as increased ON time without troublesome dyskinesia and decreased OFF time. It was also found to cause somnolence and fatigue, as well as suicidal ideation or behavior.

Recommendation: Gocovri® be non-preferred.

Clinical Criteria: Defer clinical criteria until after Osmolex ER new drug review.

Board Decision: The Board unanimously approved the above recommendation.

Osmolex® ER (amantadine extended-release); **PDL category**- Parkinson Disease-Dopaminergics/Carbidopa/Levodopa

Amantadine, the active ingredient of Osmolex® ER, is a weak uncompetitive antagonist of the NMDA receptor. Amantadine may have direct and indirect effects on dopamine neurons and it exhibits anticholinergic-like side effects. The exact mechanism by which it works is not known. It is indicated for the treatment of Parkinson's disease and for the treatment of drug-induced extrapyramidal reactions in adult patients.

Recommendation: Osmolex ® be non-preferred. Additional changes are add Amantadine HCL Caps to preferred and add Amantadine HCL Tabs to non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Lonhala® Magnair (glycopyrrolate); **PDL category**- Antiasthmatic- Anticholinergics

Glycopyrrolate, the active ingredient of Lonhala® inhalation solution, is a long-acting muscarinic antagonist, often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors M1 to M5, but in the airways, it exerts its pharmacological effect through inhibition of M3 receptor at the smooth muscle, leading to bronchodilation. It is indicated for the long-term maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. There were 2 placebo-controlled confirmatory studies of 12 weeks duration and one 48-week long-term safety study to assess the safety and efficacy of Lonhala® Magnair on lung function in adults with COPD. Both confirmatory studies were randomized, double-blind, placebo-controlled, parallel-group studies and included subjects with a clinical diagnosis of COPD, were ≥40 years of age, had a history of smoking ≥10 pack-years, and a post-bronchodilator FEV1 ≤80% of predicted. Adults also had pre-existing or concurrent cardiovascular disease and stable, background LABA ±ICS and short-acting therapy were allowed. In both studies, the mean age was 63 years, 56% were male, and 53% were current smokers with an average smoking history of 52 pack-years. The primary endpoint was the change from baseline in trough FEV1 at day 84 as compared with placebo. Results suggested that Lonhala® Magnair demonstrated a larger increase in least square mean change from baseline in trough FEV1 as compared with placebo. Compared to Lonhala® Magnair 25mcg BID, Lonhala® Magnair 50mcg BID did not provide sufficient additional benefit on a variety of endpoints, including FEV1, to support use of higher doses.

Recommendation: Lonhala® Magnair be non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Luxturna® (voretigene neparvovec-rzyl); **PDL category**- Ophthalmics- Of Interest

Luxturna® is a suspension of an adeno-associated virus vector-based gene therapy. It is a live non-replicating adeno-associated virus serotype 2 that has been genetically modified to express the human *RPE65* gene. Luxturna® is designed to deliver a normal copy of the gene encoding the human retinal pigment epithelial 65 kDa protein (RPE65) to cells of the retina in subjects with reduced or absent levels of biologically active RPE65. Mutations in the *RPE65* gene lead to reduced or absent levels of RPE65 isomerohydrolase activity, blocking the retinal cell cycle and resulting in impairment of vision. It is indicated for the treatment of patients with confirmed biallelic *RPE65* mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician(s). The safety and efficacy of Luxturna® were assessed in pediatric and adult patients with biallelic RPE65 mutation-associated retinal dystrophy (N=31) in an open-label, randomized trial.

Recommendation: Luxturna ® be non-preferred.

Clinical Criteria: Luxturna will be considered for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician(s).

Board Decision: The Board unanimously approved the above recommendation.

Lyrica CR® (pregabalin, extended-release); **PDL category**- Anticonvulsants

Pregabalin, the active ingredient of Lyrica® CR, binds with high affinity to the alpha2-delta site (an auxiliary subunit of voltage-gated calcium channels) in the CNS tissues. While the exact mechanism of action is not known, results in animals and with compounds structurally related to pregabalin (such as gabapentin) suggest that binding to the alpha2-delta subunit may be involved in pregabalin's anti-nociceptive and antiseizure effects in animals. In animal models of nerve damage, pregabalin has been shown to reduce calcium-dependent release of pro-nociceptive neurotransmitters in the spinal cord. While pregabalin is a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), it does not bind directly to $GABA_A$, $GABA_B$, or benzodiazepine receptors. Lyrica® CR is a Schedule V controlled substance and is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia. The efficacy of Lyrica® CR has not been established for the management of fibromyalgia or as adjunctive therapy for adult patients with partial onset seizures.

Recommendation: Lyrica® CR be non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Noctiva® (desmopressin acetate); **PDL category**- Vasopressins

Desmopressin acetate, the active ingredient of Noctiva®, is a synthetic analogue of 8-arginine vasopressin, an endogenous pituitary hormone also known as antidiuretic hormone (ADH). Desmopressin is a selective agonist at V2 receptors on renal cells in the collecting ducts, increasing water reabsorption in the kidneys, and reducing urine production. It is indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void. (Nocturnal polyuria was defined in the Noctiva® clinical trials as nighttime urine production exceeding one-third of the 24-hour urine production.) Before starting treatment, evaluate the patient for possible causes for the nocturia, including excessive fluid intake prior to bedtime, and optimize the treatment of underlying conditions that may be contributing to the nocturia. Confirm the diagnosis of nocturnal polyuria with a 24-hour urine collection, if one has not been obtained previously. Note that Noctiva® has not been studied in patients less than 50 years of age. The safety and efficacy of Noctiva® were assessed in two 12-week randomized, double-blind, placebo-controlled, multicenter studies that included adults ≥50 years of age with nocturia due to nocturnal polyuria. At baseline, adults were required to have a 6-month history of at least 2 nocturic episodes per night and at least 13 documented nocturia episodes over 6 nights during screening. The mean age of adults in the studies was 67 years, and 57% were men.

Recommendation: Noctiva® be non-preferred. Additional change move DDAVP Soln to preferred.

Clinical Criteria: For Noctiva: Products must be used in specified step order. Nocturnal enuresis patients will be encouraged to periodically attempt stopping DDAVP.

Board Decision: The Board unanimously approved the above recommendation.

Rhopressa® (netarsudil); **PDL category**- OP- Rho Kinase Inhibitors

Netarsudil, the active ingredient of Rhopressa®, is a rho kinase inhibitor, thought to reduce intraocular pressure (IOP) by increasing the outflow of aqueous humor through the trabecular meshwork route. However, the exact mechanism of action is not known. It is indicated for the reduction of elevated IOP in patients with open-angle glaucoma or ocular hypertension. The safety and efficacy of Rhopressa® were assessed in 3 randomized controlled trials in patients with open-angle glaucoma or ocular hypertension. While in three phase 3 studies Rhopressa® demonstrated significant reductions from baseline, it was found to be non-inferior to timolol in one study but only in the per-protocol population analysis. In another study it did not meet criteria for non-inferiority to timolol in the PP population with a maximum baseline IOP <27mmHg.

Recommendation: Rhopressa® be non-preferred.

Clinical Criteria: Add new category OP- RHO KINASE INHIBITORS. Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Segluromet® (ertugliflozin and metformin); **PDL category**- SGLT2 Inhibitors and Combinations

Segluromet® is a combination tablet containing two antihyperglycemic agents with complementary mechanisms of action to improve glycemic control. Ertugliflozin L-pyroglutamic acid is a sodium glucose co-transporter 2 (SGLT2) inhibitor. SGLT2 is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. By inhibiting SGLT2, ertugliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, thus increases urinary glucose excretion. Metformin improves glucose intolerance, lowering both basal and postprandial plasma glucose. It decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (DM) who are not adequately controlled on a regimen containing ertugliflozin or metformin, or in patients who are already treated with both ertugliflozin and metformin. It is not recommended in patients with type 1 DM or for the treatment of diabetic ketoacidosis. The safety and efficacy of ertugliflozin in combination with metformin have been studied in 4 multicenter, randomized, double-blind, placebo- or active-controlled studies that included adults with type 2 DM. There is some evidence at this time that may suggest Segluromet® may be more effective than metformin; however, there is no evidence at this time to support that Segluromet® is safer or more effective than other currently available medications, including other combination formulations or the combination of its individual agents taken together.

Recommendation: Segluromet ® be non-preferred.

Clinical Criteria: Defer until after the new drug review of Steglujan.

Board Decision: The Board unanimously approved the above recommendation.

Steglujan® (ertugliflozin and sitagliptin); **PDL category**- SGLT2 Inhibitor and Combinations

Steglujan® is a fixed combination tablet containing 2 antihyperglycemic agents with complementary mechanisms of action to improve glycemic control, including ertugliflozin L-pyroglutamic acid (a sodium glucose co-transporter 2 inhibitor or SGLT2 inhibitor) and sitagliptin (a dipeptidyl peptidase-4 inhibitor or DPP-4 inhibitor). By inhibiting SGLT2, ertugliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, and thus increases urinary glucose excretion. As a DPP-4 inhibitor, sitagliptin slows the inactivation of incretin hormones and thus increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both ertugliflozin and sitagliptin is appropriate. It is not recommended for use in patients with type 1 diabetes mellitus (DM) or for the treatment of diabetic ketoacidosis. In addition, use has not been studied in patients with a history of pancreatitis. It is not known whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Steglujan®. The safety of concomitantly administered ertugliflozin and sitagliptin was evaluated in 3 studies. Common adverse events reported with sitagliptin include upper respiratory tract infection, nasopharyngitis, headache, abdominal pain, nausea, and diarrhea. The incidence of overall and severe hypoglycemia reported with ertugliflozin 5mg plus sitagliptin was 5.3% and 0%, respectively. There have been post-marketing reports of acute pancreatitis in patients taking sitagliptin.

Recommendation: Steglujan® be non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Symdeko® (tezacaftor & ivacaftor); **PDL category**- Antiasthmatic- CFTR Potentiator & Combinations

Symdeko® is a fixed-dose combination tablet containing tezacaftor and ivacaftor that is co-packaged with ivacaftor tablets. Tezacaftor facilitates the cellular processing and trafficking of normal and select mutant forms of cystic fibrosis transmembrane conductance regulator (CFTR; including F508del-CFTR) to increase the amount of mature CFTR protein delivered to the cell surface. Ivacaftor is a CFTR potentiator that facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein at the cell surface. For ivacaftor to function CFTR protein must be present at the cell surface. Ivacaftor can potentiate the CFTR protein delivered to the cell surface by tezacaftor, leading to a further enhancement of chloride transport than either agent alone. The combined effect is increased quantity and function of CFTR at the cell surface, resulted in increases in chloride transport. It is indicated for the treatment of patients with cystic fibrosis (CF) aged 12 years and older who are homozygous for the *F508de*l mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive

to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use. The safety and efficacy of Symdeko® were assessed in CF pediatric patients ≥12 years of age in three phase 3, double-blind, placebo-controlled trials.

Recommendation: Symdeko® be non-preferred.

Clinical Criteria: Symdeko will be considered for patients with cystic fibrosis (CF) aged 12 years and older who are homozygous for the *F508de*l mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use

Board Decision: The Board unanimously approved the above recommendation.

Xhance® (fluticasone propionate); **PDL category**- Antiasthmatic- Nasal Steriods

Fluticasone propionate, the active ingredient of Xhance®, is a synthetic trifluorinated corticosteroid with anti-inflammatory activity. Fluticasone propionate has been shown in vitro to have a binding affinity for the human glucocorticoid receptor that is 18 times that of dexamethasone, twice that of the active metabolite of beclomethasone, and over 3 times that of budesonide. While the exact mechanism through which it affects nasal polyps is not known, corticosteroids have been shown to have a wide range of effects on multiple cell types (e.g. mast cells, eosinophils, lymphocytes) and mediators (e.g. histamine, cytokines, leukotrienes). It is indicated for the treatment of nasal polyps in patients 18 years of age or older. The safety and efficacy of Xhance® were assessed in two multicenter, randomized, double-blind, parallel-group, placebo-controlled dose-ranging studies that included adults with nasal polyps and associated moderate to severe nasal congestion.

Recommendation: Xhance® be non-preferred.

Clinical Criteria: Comments: All step 5 medications need to be tried before moving to step 8's. Clinical criteria: Xhance will be considered for the treatment of nasal polyps in patients 18 years of age or older. The patient has had a documented side effect, allergy, or treatment failure of two preferred nasal glucocorticoids, one of which must be fluticasone.

Board Decision: The Board unanimously approved the above recommendation.

Zilretta® (triamcinolone acetonide extended- release); **PDL category**- Glucocorticoids/ Mineralocorticoids

Triamcinolone acetonide, the active ingredient of Zilretta®, is a corticosteroid with anti-inflammatory and immunomodulating properties. It binds to and activates the glucocorticoid receptor, ultimately blocking the release of arachidonic acid and preventing the synthesis of prostaglandins and leukotrienes. It is indicated as an intra-articular injection for the management of osteoarthritis pain of the knee. It is not intended for repeat administration. The efficacy of Zilretta® was demonstrated in a multicenter, randomized, double-blind, placebo- and active-controlled study that included adults with osteoarthritis pain of the knee. The primary

efficacy endpoint comparing Zilretta® to placebo was the change from baseline at week 12 in the weekly mean of the Average Daily Pain intensity scores (ADP) as assessed by a 0-10 numeric rating scale (NRS). Results suggested that Zilretta® demonstrated a statistically significant reduction in pain intensity at the primary endpoint as compared with placebo. Also, Zilretta® demonstrated a reduction in pain intensity scores each week from weeks 1 through 12. While it was found to have a statistically significant reduction in pain intensity as compared with placebo in clinical trials, statistical significance was not demonstrated when compared to an active control of immediate-release triamcinolone in a secondary exploratory analysis.

Recommendation: Zilretta® be non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

Risk of serious and potentially fatal blood disorder prompts FDA action on oral over-the-counter benzocaine products used for teething and mouth pain and prescription local anesthetics
https://www.fda.gov/Drugs/DrugSafety/ucm608265.htm

Lamictal (lamotrigine): Drug Safety Communication - Serious Immune System Reaction
https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm605628.htm

Juluca, Tivicay, Triumeq (dolutegravir): FDA to Evaluate - Potential Risk of Neural Tube Birth Defects
https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm608168.htm?utm_campaign=FDA%20MedWatch%20-%20Juluca%2C%20Tivicay%2C%20Triumeq&utm_medium=email&utm_source=Eloqua

Keytruda (pembrolizumab) or Tecentriq (atezolizumab): FDA Alerts Health Care Professionals and Investigators: FDA Statement - Decreased Survival in Some Patients in Clinical Trials Associated with Monotherapy
https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm608253.htm

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **September 11, 2018** 5:30pm –8:30pm at the Augusta Armory.