Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

Maine Department of Health and Human Services
Office of MaineCare Services - Pharmacy Unit
11 State House Station
Augusta, Maine 04333-0011
Toll Free: (866) 796-2463; TTY: Dial 711 (Maine Relay)
Fax: (207) 287-8601

TO: Maine Drug Utilization Review Board
DATE: 03/15/2019
RE: Maine DUR Board **Meeting** minutes from March 12, 2019

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		
Jill Kingsbury, MaineCare Pharmacy Director	X		

Guests of the Board: Ed Bosshart, PharmD, Gordon Smith, Esq

CALL TO ORDER: 5:30PM

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

PUBLIC COMMENTS

Robert Mead from Pfizer: Highlighted the attributes of Daurismo and Lorbrena.
Jan Gou from Otsuka: Highlighted the attributes of Abilify Mycite.

OLD BUSINESS

DUR MINUTES

The December DUR meeting minutes were accepted as written.

A provider proposed to the State requesting that the restriction on the Hepatitis C PA form: Prescriber is, or has consulted with, a gastroenterologist, hepatologist, ID specialist or other Hepatitis specialist. Consult must be w/in the past year with documentation of recommended regimen be lifted.

Board Decision: No action at this time. Change Healthcare will prepare data for review at the June meeting.

MAINECARE UPDATE

Jill Kingsbury announced the appointment of the following:
Michelle Probert new Director of MaineCare
Gordon Smith new Director of Opioid Response.

NEW BUSINESS

REVIEWS ON BIOSIMILARS

Change Healthcare will no longer provider New Drug Reviews on Biosimilars.

DATA PRESENTATION: VIVITROL ADHERENCE

The opioid epidemic has resulted in a dramatic increase in the use of abuse deterrent medications, the most common being the agonist/antagonist combination of buprenorphine and naloxone, given in an oral form daily. There are also depot intramuscular formulations of buprenorphine and naltrexone, each given once every 28 days. Two recent trials comparing daily sublingual buprenorphine with monthly LAI naltrexone found minimal differences in abstinence rates but may offer advantages for patients who do not respond to agonist treatment, cannot adhere to a daily medication, or are in a safety-sensitive occupation that does not permit concurrent agonist treatment. However, trials of LAI naltrexone have been limited by high dropout rates and the transition on to LAI naltrexone may be a challenge for some patients. As an example, a 2011 trial compared a once-monthly, injectable depot formulation of naltrexone with placebo in 250 patients with a DSM-IV diagnosis of opioid dependence over 24 weeks, finding that the median proportion of weeks of confirmed abstinence was greater in the actively treated group compared with the placebo group (90 versus 35 percent); however, these findings excluded 47 percent of the patients who did not complete the study. Treatment with oral or LAI naltrexone is a reasonable first-line alternative to methadone or buprenorphine in those who have a mild opioid use disorder, require medical supervision or are in occupations where opioid agonist treatment is not allowed (public safety, transport of hazardous materials, etc.).

Identify members given at least one dose of IM naltrexone and look to see how may consecutive doses were given monthly, without any interruption. We will follow each member out from the first prescription to the end of calendar year 2017, allowing us to assess the percentage of members who were adherent with therapy. We will also look at member profiles to see if an alternative therapy was trialed after the last LAI naltrexone prescription was filled.

From the data, adherence to opiate receptor antagonists is poor, in both oral and IMformulations. Naltrexone orally is used for other conditions off label including impulse control disorders and self-injurious behavior, as examples. Off label use may explain the absence of a diagnosis of opiate or alcohol abuse disorder for 78 patients on oral naltrexone and 3 on IM.

Consistent with general clinical impressions, adherence and treatment persistence is poor for either orally or intramuscularly administered naltrexone. Notably, only one patient with opiate dependence persisted with IM naltrexone treatment beyond 8 weeks.

Board Decision: No action needed at this time.

INTRODUCATION: CONTINUOUS USE OF ANTIDEPRESSANTS AT 3, 6 AND 12 MONTHS AFTER INITIATION

The use of antidepressants is common in MaineCare members and they are used to treat both unipolar and bipolar depression as well as anxiety disorders. The lifetime prevalence of major depressive disorder is 16 %. %. The World Health Organization has determined that depression is the 11th greatest cause of disability and mortality in the world. In the US population it is 2nd among all diseases and injuries for disability and is highly recurrent, with rates upwards of 40% at 2 years and 75% in patients at 5 years who have had two or more previous depressive episodes. Clinical trials and meta-analysis have been conducted comparing the various antidepressants, but there is general agreement that there is not one preferred class of medication, or within a class, one preferred drug. Additionally, adherence tends to be poor in patients treated by primary care providers. It is generally advised that patients also receive behavioral therapy and with certain diagnoses, such as bipolar depression, patients will need to be on other mood stabilizing drugs to prevent escalation into mania. Initiation of antidepressant therapy typically involves a gradual increase in the dose of antidepressant, sometimes switching to an alternative agent based on the side effects of the initial drug. The continuation phase of treatment generally lasts from 9-12 months, with many patients progressing on to maintenance therapy.

We will use paid, non-reversed Medicaid pharmacy and medical claims date from CYY 2017 excluding members with Part D, MaineRX and TPL. Identify members with at least one prescription for an antidepressant (SSRIs, SNRIs, TCAs, MAOIs, atypical antidepressants, serotonin modulators). For each, look at duration of therapy at time points 3,6 and 12 months, switches to other antidepressants, co-administration of other antidepressants and diagnosis. For those with bipolar depression, identify if members are on other recommended mood stabilizing drugs concomitantly.

Board Decision: No action needed at this time.

NEW DRUG REVIEW

Abilify® Mycite (aripiprazole); **PDL category-** Antipsychotics- Atypical

Aripiprazole, the active ingredient of Abilify® Mycite, is an atypical antipsychotic. While the mechanism is not known, it is thought to be mediated through a combination of partial agonist activity at the D2 and 5-HT1A receptors as well as antagonist activity at 5-HT2A receptors. It is indicated as a drug-device combination product comprised of aripiprazole tablets embedded with an Ingestible Event Marker (IEM) sensor intended to tract drug ingestion, is indicated for the:

- Treatment of adults with schizophrenia
- Treatment of bipolar 1 disorder
    - Acute treatment of adults with manic and mixed episodes as monotherapy and as adjunct to lithium or valproate
    - Maintenance treatment of adults as monotherapy and as adjunct to lithium or valproate

- Adjunctive treatment of adults with Major Depressive Disorder (MDD)

The concomitant use of aripiprazole with strong CYP3A4 (e.g. itraconazole, clarithromycin) or strong CYP2D6 inhibitors (e.g. quinidine, fluoxetine, paroxetine) increased the exposure of aripiprazole compared to the use of aripiprazole alone. Abilify® Mycite has a box warning regarding increased mortality in elderly patients with dementia-related psychosis, as well as suicidal thoughts and behaviors. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. The safety and efficacy of aripiprazole tablets for the treatment of adults with schizophrenia, acute treatment of adults with manic and mixed episodes associated with bipolar I disorder, and adjunctive treatment of adults with MDD have been established and is based on numerous adequate and well-controlled trials of aripiprazole tablets. The studies in the Abilify® Mycite clinical trials section were the same as in the clinical trials section of Abilify® tablets, with the exception of the pediatric trials, as Abilify® Mycite is not indicated for the pediatric population. Abilify® tablets and its generic version have been available for numerous years and have been shown to be safe and effective.

Recommendation: Abilify® Mycite be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Arikayce® (amikacin liposome inhalation suspension); **PDL category**- Amino glycosides

Amikacin sulfate, the active ingredient of Arikayce®, is an aminoglycoside antibacterial. It is a polycationic, semisynthetic bacterial aminoglycoside that enters the bacterial cell by binding to negatively charged components of the bacterial cell wall, disrupting the overall architecture of the cell wall. The main mechanism of action is the disruption and inhibition of protein synthesis in the target bacteria by binding to the 30S ribosomal subunit. The mechanism of resistance to amikacin in mycobacteria has been linked to mutations in the rrs gene of the 16S rRNA. In clinical trials, *Mycobacterium* avium complex (MAC) isolates developing an amikacins MIC of >64mcg/ml after baseline were observed in a higher proportion of subjects treated with Arikayce®. It is indicated for in adults who have limited or no alternative treatment options, for the treatment of *Mycobacterium* avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. As only limited clinical safety and effectiveness data for Arikayce® are currently available, reserve Arikayce® for use in adults who have limited or no alternative treatment options. This drug is indicated for use in a limited sand specific population of patients. This indication is approved under accelerated approval based on achieving sputum culture conversion (defined as 3 consecutive negative monthly sputum cultures) by month 6. Clinical benefit has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The safety and efficacy of Arikayce® were assessed in an open-label, randomized, multicenter study that included adults with refractory *Mycobacterium avium* complex (MAC) lung disease as confirmed by at least 2 sputum culture results. The endpoint for assessing efficacy was based on achieving culture conversion (3 consecutive monthly negative sputum cultures) by month 6. The date of conversion was defined as the date of the first of the 3 negative monthly cultures, which had to be achieved by month 4 in order to meet the endpoint by month 6. Results suggested that the proportion achieving culture conversion by month 6 was significantly greater ($p<0.0001$) for Arikayce® plus background regimen (N=65/224, 29%) as compared to background regimen alone.

Recommendation: Arikayce® be non-preferred.

Clinical Criteria: Clinical PA to verify appropriate diagnosis. Arikayce will require clinical PA to confirm MAC lung disease and for use in adults who have limited or no alternative treatment options.

Board Decision: The Board unanimously approved the above recommendation.

Bryhali® (halobetasol); **PDL category**- Topical – Corticosteroids, Very High Potency

Halobetasol propionate, the active ingredient of Bryhali®, is a corticosteroid. Corticosteroids play a role in cellular signaling, immune function, inflammation, and protein regulation; however, the exact mechanism of action when used for its indication is not known. In healthy subjects, a vasoconstrictor assay with Bryhali® lotion indicated that the formulation is in the potent to super-potent range of potency as compared to other topical corticosteroids. It is indicated for the topical treatment of plaque psoriasis in adults. The safety and efficacy of Bryhali lotion were assessed in 2 prospective, multicenter, randomized, double-blind studies that included adults 18 years of age and older (N=430) with moderate to severe plaque psoriasis that covered a BSA between 3% and 12%, excluding the face, scalp, palms, soles, axillaie, and intertriginous areas. Treatment was given for up to 8 weeks, and subjects had a follow-up visit 4 weeks after the end of treatment (week 12). It was found to be in the potent to super-potent range of potency as compared to other topical corticosteroids. Compared with vehicle, Bryhali® was found to be significantly more effective for IGA treatment success in adults with moderate-to-severe plaque psoriasis.

Recommendation: Bryhali® be non-preferred.

Clinical Criteria:

- At least 1 drug from each potency of 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.

Copiktra® (duvelisib); **PDL category**- Cancer

Duvelisib, the active ingredient of Copiktra®, is an inhibitor of P13K expressed in normal and malignant B-cells. It induced growth inhibition and reduced viability in cell lines derived from malignant B-cells and in primary chronic lymphocytic leukemia tumor cells. Duvelisib inhibits several key cell-signaling pathways, including B-cell receptor signaling and CXCR12-mediated chemotaxis of malignant B-cells. In addition, duvelisib inhibits CXCL12-induced T cell migration and M-CSF and IL-4 driven M2 polarization of macrophages. It is indicated for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least 2 prior therapies. For the treatment of adults with relapsed or refractory follicular lymphoma (FL) after at least 2 prior systemic therapies. This indication is approved under accelerated approval based on overall response rate (ORR); continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. It was found to be significantly more effective than vehicle for the co-primary endpoint of the proportion with a ≥4-point improvement form baseline in the weekly mean ASDD

item #2 in both studies, as well as a statistically significant difference favoring Qbrexza® as compared with the vehicle for mean absolute change from baseline in sweat production in study 2.

Recommendation: Copiktra® be non-preferred.

Clinical Criteria:

- Copiktra will be considered for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least 2 prior therapies AND the treatment of adults with relapsed or refractory follicular lymphoma (FL) after at least 2 prior systemic therapies. This indication is approved under accelerated approval based on overall response rate (ORR); continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Board Decision: The Board unanimously approved the above recommendation.

Cequa® (cyclosporine); **PDL category**- OP. – Of Interest

Cyclosporine, the active ingredient of Cequa®, is a topical ophthalmic solution. When cyclosporine is administered systemically, it is a calcineurin inhibitor immunosuppressant agent. Topical administration of cyclosporine is thought to act as a partial immunomodulator; however, the exact mechanism of action is not known. It is indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye). The efficacy of Cequa® was assessed in 2 multicenter, randomized, well-controlled studies that included adults with keratoconjunctivitis sicca. In clinical trials, there was a statistically significant higher percentage of eyes with increases of ≥10 mm from baseline in Schirmer wetting. There is no evidence found to suggest Cequa® is safer or more effective than other currently preferred, more cost-effective medications, including artificial tears.

Recommendation: Cequa® be non-preferred.

Clinical Criteria:

- Must fail adequate trials of multi agents from artificial tears and lubricant category.

Board Decision: The Board unanimously approved the above recommendation.

Daurismo® (glasdegib); **PDL category**- Cancer

Glasdegib, the active ingredient of Daurismo®, is a potent small molecule inhibitor of Smoothened (SMO). It is an inhibitor of the Hedgehog pathway that binds to and inhibits SMO, a transmembrane protein involved in hedgehog signal transduction. In animal studies, glasdegib in combination with low-dose cytarabine inhibited increases in tumor size and reduced the percentage of CD45+/CD33+ blasts in the marrow to a greater extent than either treatment alone. It is indicated in combination with low-dose cytarabine, for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are ≥75 years old or who have comorbidities that preclude use of intensive induction chemotherapy. Daurismo® has not been studied in patients with the comorbidities of severe renal impairment or moderate-to-severe hepatic impairment. The efficacy of Daurismo® in combination with low-dose cytarabine was assessed in a multicenter, randomized, open-label study that included adults ≥55 years of age with newly-diagnosed

AML (N=115) who met at least one of the following criteria: age ≥75 years; severe cardiac disease; baseline Easter Cooperative Oncology Group (ECOG) performance status of 2; or baseline serum creatinine >1.3mg/dl. It has not been studied in patients with comorbidities of severe renal impairment or moderate-to-severe hepatic impairment. QTc interval prolongation and ventricular arrhythmias can develop during treatment. It is recommended to monitor ECGs and electrolytes. In an open-label study, Daurismo® plus low-dose cytarabine were superior compared to low-dose cytarabine alone for overall survival.

Recommendation: Daurismo® be non-preferred.

Clinical Criteria:

- Daurismo will be considered in combination with low-dose cytarabine, for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are ≥75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.

Board Decision: The Board unanimously approved the above recommendation.

Galafold® (migalastat); **PDL category**- Fabry Disease Agents

Migalastat, the active ingredient of Galafold®, is an alpha-galactosidase (alpha-Gal A), pharmacological chaperone that reversibly binds to the active site of the alpha-GAL A protein (encoded by the galactosidase alpha gene, GLA), which is deficient in Fabry disease. This binding stabilizes alpha-Gal A, allowing its trafficking from the endoplasmic reticulum into the lysosome, where it exerts its action. In the lysosome, at a lower pH and at a higher concentration of relevant substrates, migalastat dissociates from alpha-Gal A, allowing it to break down the glycosphingolipids globotriaosylceramide (GL-3) and globotriaosylsphingosine (lyso-Gb-3). Certain GLA variants, or mutations, causing Fabry disease result in the production of abnormally folded and less stable forms of the alpha-Gal A protein retain enzymatic activity however. Those GLA variants, referred to as amenable variants, produce alpha-Gal A proteins that may be stabilized by migalastat, thus restoring their trafficking to lysosomes and their intralysosomal activity. Indicated for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data. This medication is approved under accelerated approval based on reduction in kidney interstitial capillary cell globotriaosylceramide (KIC GL-3) substrate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The safety and efficacy of Galafold® were assessed in a 6-month randomized, double-blind, placebo-controlled, phase followed by a 6-month open-label treatment phase and a 12-month open-label extension phase. This medication was approved under accelerated approval based on reduction in kidney interstitial capillary cell globotriaosylceramide (KIC GL-3) substrate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Recommendation: Galafold® 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.

Inveltys® (loteprednol etabonate); **PDL category**- OP-Anti-inflammatory/Steroids Ophth.

Loteprednol etabonate, the active ingredient of Inveltys®, is a corticosteroid. Corticosteroids inhibit the inflammatory response to a variety of inciting agents and probably delay or slow healing. They inhibit the edema, fibrin deposition, capillary dilation, leukocyte migration, capillary proliferation, fibroblast proliferation, deposition of collagen, and scar formation associated with inflammation. It is indicated for the treatment of post-operative inflammation and pain following ocular surgery. The efficacy of Inveltys® was assessed in 2 multicenter, randomized, double-masked, placebo-controlled studies where patient with an anterior cell grade ≥2 after cataract surgery were randomized to Inveltys® or placebo after surgery. Complete resolution of inflammation (a cell count of 0 maintained through day 15 without rescue medication) and complete resolution of pain (a patient-reported pain grade of 0 maintained through day 15 without rescue medication) was assessed 4, 8, and 15 days post-surgery. Results suggested that in the intent-to-treat analysis of both studies, a significant benefit was seen in the Inveltys® group for complete resolution of ocular inflammation at days 8 and 15, and complete resolution of pain at days 4, 8, and 15 when compared with placebo. Lotemax® products, including the gel and ointment, carry the same indication as Inveltys®. Lotemax® does not have a generic version available for the gel or ointment. Lotemax® suspension is only indicated for post-operative inflammation after ocular surgery, not pain. All Lotemax® dosage forms are to be administered 4 times daily, while Inveltys® is approved to be administered twice-daily.

Recommendation: Inveltys® 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.

Lorbrena® (lorlatinib); **PDL category**- Cancer

Lorlatinib, the active ingredient of Lorbrena®, is a kinase inhibitor. It is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on

- Crizotinib and at least one other ALK inhibitor for metastatic disease; OR
- Alectinib as the first ALK inhibitor therapy for metastatic disease; OR
- Ceritinib as the first ALK inhibitor therapy for metastatic disease

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. The efficacy of Lorbrena® was assessed in a subgroup of patients with ALK-positive metastatic NSCLC previously treated with one or more ALK kinase inhibitors who were enrolled in a non-randomized, dose-ranging and activity-estimating, multicenter study. This indication is

approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. In a subgroup of patients with ALK-positive metastatic NSCLC previously treated with one or more ALK kinase inhibitors (N=215), 48% had overall response rate and 44% had partial response.

Recommendation: Lorbena® be non-preferred.

Clinical Criteria:

- Lorbrena will be considered for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on Crizotinib and at least one other ALK inhibitor for metastatic disease; OR Alectinib as the first ALK inhibitor therapy for metastatic disease; OR Ceritinib as the first ALK inhibitor therapy for metastatic disease.

Board Decision: The Board unanimously approved the above recommendation.

Panzyga® (immune globulin intravenous (IVIG), human-ifas); **PDL category-** Immune Globulin Intravenous

Immune globulin intravenous (IVIG; Human), the active ingredient of Panzyga®, is a solvent/detergent (S/D)-treated, sterile preparation of highly purified immunoglobulin G (IgG) derived from large pools of human plasma. Panzyga® contains only trace amounts of sodium; it contains glycine but no preservatives or sucrose. Panzyga® also contains a broad spectrum of IgG antibodies against bacterial and viral agents that are capable of opsonization and neutralization of microbes and toxins. All units of human plasma used in the manufacturer of Panzyga® are provided by FDA-approved blood and plasma establishments and are tested by FDA-licensed serological tests for HBsAg, antibodies to HCV and HIV and Nucleic Acid Test (NAT) for HCV and HIV-1 and found to be non-reactive (negative). The product is manufactured by cold ethanol fractionation process followed by purification methodologies, as well as D/D treatment and nanofiltration. It is indicated for the treatment of:

- Primary humoral immunodeficiency (PI) in patients 2 years of age and older. This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies
- Adults with chronic immune thrombocytopenia (ITP) to raise platelet counts to control or prevent bleeding

Study 1 was a prospective, open-label, single-arm, multicenter study that included children and adults with PI who were received Panzyga® every 3 to 4 weeks for a mean of 360 days. The mean age of subjects was 26.8 years (range 2 to 65 years). The primary endpoint was the number of episodes of serious bacterial infections per patient per year. Serious infections included pneumonia, bacteremia or sepsis, osteomyelitis/septic arthritis, visceral abscesses, or bacterial meningitis. Secondary outcomes were also assessed. For the primary endpoint, the observed rate was 0.08 serious bacterial infections per patient per year (4 infections over 50.2 patient-years). There is no evidence at this time to support that Panzyga® is safer or more effective than the currently available, more cost-effective medications.

Recommendation: Panzyga® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation**.**

Qbrexza® (glycopyrronium tosylate); **PDL category-** Topical- Astringent/Protectants

Glycopyrronium, the active ingredient of Qbrexza®, is a competitive inhibitor of acetylcholine receptors that are located on certain peripheral tissues, including sweat glands. In hyperhidrosis, glycopyrronium inhibits the action of acetylcholine on sweat glands, reducing sweating. It is indicated for the topical treatment of primary axillary hyperhidrosis in adult and pediatric patients 9 years of age and older. For topical use in the underarm area only and not for use in other body areas. Apply to clean dry skin and do not use more frequently than once every 24 hours. The safety and efficacy of Qbrexza® were assessed in 2 randomized, vehicle-controlled multicenter trials that included subjects with primary axillary hyperhidrosis aged 9 years or older.

Recommendation: Qbrexza® 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**.**

Siklos® (hydroxyurea); **PDL category-** Sickle Cell Disease

Hydroxyurea, the active ingredient of Siklos®, is an antimetabolite. The mechanisms by which Siklos® produces its benefits in patients with sickle cell anemia are not certain. Known effects of Siklos® which may contribute to its beneficial effects including increasing hemoglobin F levels in red blood cells (RBCs), decreasing neutrophils, increasing the water content of RBCs, increasing deformability of sickled cells, and altering the adhesion of RBCs to endothelium. The correlation between hydroxyurea concentrations, reduction of crisis rate, and increase in hemoglobin F is not known. It is indicated to reduce the frequency of painful crises and to reduce the need for blood transfusions in pediatric patients 2 years of age and older, with sickle cell anemia with recurrent moderate to severe painful crises. The efficacy of Siklos® was assessed in the European Sickle Cell Disease Cohort study (ESCORT HU), which was an open-label single-arm study that included pediatric patients (N=405) from 2-18 years of age with sickle cell disease, of which 141 had not been previously treated with hydroxyurea prior to enrollment. Evaluable patients had at least 12 months follow-up. There is no evidence found to suggest Siklos® is safer or more effective than other currently preferred, more cost-effective medications.

Recommendation: Siklos® be non-preferred.

Clinical Criteria:

- Add Hydroxyurea to preferred in the Sickle Cell Disease category.

Board Decision: The Board unanimously approved the above recommendation**.**

Symjepi® (epinephrine injection); **PDL category-** Anaphylactic Devices

Epinephrine, the active ingredient of Symjepi®, acts on both alpha and beta-adrenergic receptors. Through its action on alpha-adrenergic receptors, epinephrine lessens the vasodilation and increased vascular permeability that occurs during anaphylaxis, which can lead to loss of intravascular fluid volume and hypotension. Through its action on beta-adrenergic receptors, epinephrine causes bronchial smooth muscle relaxation and helps alleviate bronchospasm, wheezing, and dyspnea that may occur during anaphylaxis. In addition, epinephrine alleviates pruritus, urticaria, and angioedema, and may relieve gastrointestinal and genitourinary symptoms associated with anaphylaxis due to its relaxer effects on the smooth muscle of the stomach, intestine, uterus, and urinary bladder. It is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g. order Hymenoptera, which includes bees, wasps, hornets, yellow jackets, and fire ants) and biting insects (e.g. Triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g. radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis. Symjepi® is intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions. Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea, and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria, or angioedema. It is intended for immediate administration as emergency supportive therapy only and is not a substitute for immediate medical care. There were no clinical trials in the prescribing information of Symjepi®. Other auto-injectable epinephrines are available, including a generic version. Epinephrine is the drug of choice for the treatment of anaphylaxis and should be administered as soon as anaphylaxis is recognized.

Recommendation: Symjepi® 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**.**

Sympazan® (clobazam); **PDL category**- Anticonvulsants

Clobazam, the active ingredient of Sympazan®, is a benzodiazepine derivative. The exact mechanism of action is not fully understood, but it is thought to involve potentiation of GABAergic neurotransmission resulting from binding at the benzodiazepine site of the GABA-A receptor. Sympazan® is a Schedule IV controlled substance. It can be abused in a similar manner as other benzodiazepines such as diazepam. It is indicated for the adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in patients 2 years of age and older. The efficacy of Sympazan® is based upon bioavailability studies comparing clobazam tablets to Sympazan®. Sympazan® oral films at single doses of 10mg and 20mg clobazam have been shown to be bioequivalent (Cmax and AUC) to clobazam tablets at equivalent doses. The efficacy of Sympazan® is based upon bioavailability studies comparing clobazam tablets with Sympazan® oral films. Sympazan® was approved on the basis of its similar bioavailability to clobazam tablets, which are considerably less costly.

Recommendation: Sympazan® be non-preferred.

Clinical Criteria:

- Add Clobazam to preferred in the Anticonvulsants.

Board Decision: The Board unanimously approved the above recommendation.

Tiglutik® (riluzole); **PDL category-** ALS Drugs

Riluzole, the active ingredient of Tiglutik®, is a member of the benzothiazole class. The exact mechanism of action by which riluzole exerts its therapeutic effects in patients with amyotrophic lateral sclerosis (ALS) is not known. It is for the treatment of amyotrophic lateral sclerosis (ALS). In clinical trials with ALS patients, patients on concomitant medications which were potentially hepatotoxic (e.g. allopurinol, methyldopa, sulfasalazine) were excluded. Tiglutik®-treated patients who take other hepatotoxic drugs may be at an increased risk for hepatotoxicity. The efficacy of Tiglutik® is based upon bioavailability studies comparing oral riluzole tablets to Tiglutik® oral suspension. The efficacy of riluzole was assessed in 2 studies that evaluated 50mg tablets BID in patients with ALS. Both studies included patients with either familial or sporadic ALS, disease duration of less than 5 years, and baseline forced vital capacity ≥60% of normal. Both studies were randomized, double-blind, placebo-controlled studies. Tiglutik® was approved on the basis of its similar bioavailability to riluzole tablets. While this preformulated thickened suspension may be more convenient than crushing riluzole tablets, which patients have been doing for some time, Tiglutik® is prohibitively priced at more than 30X the cost of riluzole tablets. It is therefore recommended that Tiglutik® remain non-preferred and require prior authorization and be available only to those who are unable to take whole or crushed riluzole tablets.

Recommendation: Sympazan® be non-preferred.

Clinical Criteria:

- Add Clobazam to preferred in the Anticonvulsants.

Board Decision: The Board unanimously approved the above recommendation.

Tiglutik® (itraconazole); **PDL category**-

Itraconazole, the active ingredient of Tolsura®, is an azole antifungal agent. It has been shown in vitro to inhibit the cytochrome P450-dependent, C-demethylation of ergosterol, which is a vital component of fungal cell membranes. Isolates from several fungal species with decreased susceptibility to itraconazole have been isolated in vitro and from patients receiving prolonged therapy. It is indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised adult patients:

- Blastomycosis, pulmonary, and extrapulmonary
- Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and
- Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy

Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted

before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-fungal therapy should be adjusted accordingly. Tolsura® is not indicated for the treatment of onychomycosis. Tolsura® is not interchangeable or substitutable with other itraconazole products due to the differences in the dosing between Tolsura® and other itraconazole products. Therefore, follow the specific dosage recommendations for Tolsura®. Clinical studies in the clinical trials section of the prescribing information for Tolsura® were conducted with itraconazole 100mg capsules. Results of the small open-label studies for blastomycosis, histoplasmosis, and aspergillosis demonstrated substantial evidence of the efficacy of itraconazole capsules as compared with the natural history of untreated cases. Itraconazole products, including brand and generics, have been available for numerous years. Dosage for Tolsura® is different from that of other itraconazole formulations. Tolsura® is not interchangeable or substitutable with other itraconazole products.

Recommendation: Tolsura® 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.

Xelpros® (latanoprost ophthalmic emulsion); **PDL category**-

Latanoprost, the active ingredient of Xelpros®, is a prostaglandin F2α analogue. It is thought to reduce the intraocular pressure (IOP) by increasing the outflow of aqueous humor. Studies in humans and in animals suggest that the main mechanism of action is increased uveoscleral outflow. Elevated IOP is a major risk factor for glaucomatous field loss; the higher the IOP, the greater chance of optic nerve damage and visual field loss. It is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. Limited information was found in the clinical trials section for Xelpros®. In randomized, controlled clinical trials including patients with open angle glaucoma or ocular hypertension with mean baseline IOP of 23-6mmHg, the mean IOP-lowering effect of Xelpros® given once daily in the evening was up to 6-8mmHg. There is no evidence that Xelpros® is safer or more effective than the currently available, more cost-effective medications.

Recommendation: Xelpros® 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.

Xerava® (eravacycline); PDL category- Tetracyclines

Eravacycline, the active ingredient of Xerava®, is a synthetic tetracycline-class antibacterial agent. It disrupts bacterial protein synthesis by binding to the 30S ribosomal subunit, thus preventing the incorporation of amino acid residues into elongating peptide chains. It is indicated for the treatment of complicated intra-abdominal infections (cIAI) caused by susceptible microorganisms: *Escherichia coli, Klebsiella pneumoniae, Citrobacter freundii, Enterobacter cloacae, Klebsiella oxytoca, Enterococcus faecalis, Enterococcus faecium, Staphylococcus aureus, Streptococcus anginosus* group, *Clostridium perfringens, Bacteroides species*, and *Parabacteroides distasonis* in patients 18 years or older. It is not indicated for the treatment of complicated urinary tract infections (cUTIs). To reduce the development of drug-resistant bacteria and maintain the effectiveness of Xerava® and other antibacterial drugs, Xerava® should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy. The safety and efficacy of Xerava® were assessed in 2 phase 3, randomized, double-blind, active-controlled multicenter studies that included patients with complicated intra-abdominal infections (cIAI), which included appendicitis, cholecystitis, diverticulitis, gastric/duodenal perforation, intra-abdominal abscess, perforation of intestine, and peritonitis. In clinical trials, it was found to be comparable to ertapenem and meropenem for achieving clinical cure rates; however, based on pooled phase 3 information, Xerava® was found to have higher clinical cure rates at the test of cure compared with ertapenem or meropenem with certain baseline pathogens. Xerava® has been shown to be non-inferior to carbapenems (ertapenem, meropenem) in achieving clinical cure of complicated intra-abdominal infections. To minimize the development of resistance to this new antibiotic, it should be non-preferred, and its use limited to those patients with complicated intra-abdominal infections that are resistant to existing antibiotics, as well as in patients who cannot tolerate existing antibiotics.

Recommendation: Xerava® 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.

Xospata® (gilteritinib); **PDL category**- Cancer

Gilteritinib, the active ingredient of Xospata®, is a tyrosine kinase inhibitor. It is a small molecule that inhibits multiple receptor tyrosine kinases, including FMS-like tyrosine kinase 3 (FLT3). It demonstrated the ability to inhibit FLT3 receptor signaling and proliferation in cells exogenously expressing FLT3, as well as induced apoptosis in leukemic cells expressing FLT3-ITD. It is indicated for the treatment of adults who have relapsed or refractory acute myeloid leukemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test. The efficacy of Xospata® was assessed in a study that included adult patients with relapsed or refractory AML having a FLT3, ITD, D835, or I836 mutation. Xospata was given until unacceptable toxicity or lack of clinical benefit. The median age of adults in the study (the ADMIRAL trial) was 60 years, and 46% were male. In addition, 59% had untreated relapse AML and 41% had primary refractory AML. In a clinical trial, almost 12% on Xospata® achieved complete remission.

Recommendation: Xospata® be non-preferred.

Clinical Criteria:

- Xospata will be considered for the treatment of adults who have relapsed or refractory acute myeloid leukemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test.

Board Decision: The Board unanimously approved the above recommendation.

Xyosted® (testosterone enanthate); **PDL category**- Androgens/Anabolic

Testosterone enanthate, the active ingredient of Xyosted®, is an ester derivative of the endogenous androgen testosterone. Endogenous androgens, including testosterone, are responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. Xyosted® is a Schedule III controlled substance. It is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

- Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

The safety and efficacy of Xyosted® in adult males with 'age-related hypogonadism' (also referred to as 'late-onset hypogonadism') have not been established. The safety and efficacy of Xyosted® in males less than 18 years of age have not been established. Xyosted® has a box warning regarding blood pressure increases. Xyosted® can cause blood pressure increases that can increase the risk for major adverse cardiovascular events (MACE), including non-fatal MI, non-fatal stroke, and cardiovascular death, with greater risk for MACE in patients with cardiovascular risk factors or established cardiovascular disease. The safety and efficacy of Xyosted® were assessed in a 52-week, open-label study that included adult males with hypogonadism. In clinical studies, Xyosted® was found to deliver physiologic amounts of testosterone, producing circulating testosterone levels that approximate normal concentrations (of 300-1100ng/dL) in healthy men.

Recommendation: Xyosted® be 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. Additionally, laboratory evidence of a testosterone deficiency must be supplied. One of each dosage form should be tried (tablet, injection, and topical).

Board Decision: The Board unanimously approved the above recommendation.

Yupelri® (revefenacin); **PDL category**-

Revefenacin, the active ingredient of Yupelri®, is a long-acting muscarinic antagonist, which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors M1 to M5. In the airways, it exhibits its pharmacological effects through inhibition of the M3 receptors at the smooth muscle, leading to bronchodilation. It is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). The safety and efficacy of Yupelri® were assessed in 2 dose-ranging studies, 2 replicate 12-week, phase 3 confirmatory studies, and a 52-week safety trial. The efficacy of Yupelri® is mainly based on the two replicate, phase 3 placebo-controlled confirmatory trials. Yupelri® is the first and only once-daily inhaled bronchodilator FDA approved for COPD. Lonhala® Magnair is an inhaled long-acting bronchodilator indicated for COPD and it is the first nebulized long-acting antimuscarinic approved but is to be used twice daily. Yupelri® has been found to be effective for COPD treatment as compared with placebo; however, no comparator trials with other active ingredients have been found.

Recommendation: Yupelri® 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.

Zemdri® (plazomicin); **PDL category**- Aminoglycosides

Plazomicin, the active ingredient of Zemdri®, is a semi-synthetic aminoglycoside antibacterial derived from sisomicin. It acts by binding to bacterial 30S ribosomal subunit, thus inhibiting protein synthesis. It is indicated for the the treatment of complicated urinary tract infections (cUTI), including pyelonephritis caused by the following susceptible microorganism(s): *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis*, and *Enterobacter cloacae*. As only limited clinical safety and efficacy data for Zemdri® are currently available, reserve Zemdri® for use in cUTI patients who have limited or no alternative treatment options. The safety and efficacy of Zemdri® were assessed in a multicenter, double-blind, non-inferiority study that included adults hospitalized with cUTI, including pyelonephritis (N=609) who were randomized to Zemdri® or meropenem (1g IV Q8H as a 30-minute infusion). As only limited clinical safety and efficacy date for Zemdri are currently available, reserve Zemdri for use in cUTI patients who have limited or no alternative treatment options. In a clinical trial comparing Zemdri with meropenem, Zemdri® was found to demonstrate efficacy and be as effective as meropenem for composite cure at day 5 and test of cure.

Recommendation: Zemdri® be non-preferred.

Clinical Criteria:

- Zemdri will be reserved for patients with limited or no alternative treatment of care.

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

FDA analysis finds no new or unexpected safety risks associated with Nuplazid (pimavanserin), a medication to treat the hallucinations and delusions of Parkinson's disease psychosis
https://www.fda.gov/Drugs/DrugSafety/ucm621160.htm?utm_campaign=FDA%20analysis%20finds%20no%20new%20or%20unexpected%20safety%20risks%20associated%20with%20Nuplazid&utm_medium=email&utm_source=Eloqua

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **June 11, 2019** 5:30pm –8:30pm at the Augusta Armory.