PAUL R. LEPAGE
GOVERNOR

Maine Department of Health and Human Services
MaineCare Services
Pharmacy Unit
11 State House Station
Augusta, Maine 04333-0011

BETHANY L. HAMM
ACTING COMMISSIONER

TO: Maine Drug Utilization Review Board
DATE: 9/14/2018
RE: Maine DUR Board **Meeting** minutes from September 11, 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, Jeff Caulfield, Lead Epidemiologist for Viral Infections from CDC: Discussed HCV treatment.

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 Retacrit.
Jane Guo from Otsuka: Highlighted the attributes of Jynarque.

OLD BUSINESS

DUR MINUTES

The June DUR meeting minutes were accepted as written.

MAINECARE UPDATE

No update at this time.

NEW BUSINESS

INTRODUCTION: USE OF CHRONIC TRIPTANS

The use of triptans has become standard of care for the treatment of acute migraine headaches, given their effectiveness, safety and tolerability. However, like many medications used to treat migraine, overuse renders them less effective. Additionally, rebound headaches from triptan overuse is common. For patients who experience frequent headaches, or whose headaches are long lasting or chronic, use of headache prophylactic medications are recommended by several medical associations, including the American Headache Society and the American Academy of Neurology. While there may be slight variation in the definitions, generally prophylaxis is recommended for patients who experience more than 4 migraine headaches a month, or those in whom headaches last more than 12 hours. In patients with chronic migraines, those who have 15 or more headache days per month, the focus primarily should be on finding a suitable prophylactic medication in order to minimize the incidence of acute headaches that require treatment with triptans or other medications. Botox is a prophylactic injectable treatment given to patients with refractory migraines, despite trying other prophylaxis and is effective in decreasing acute migraine attacks.

Change Healthcare will identify members with triptan prescriptions of more than 9 doses every 30 days for greater than or equal to 90 days and examine whether they are also taking medications, such as beta blockers, antidepressants or anticonvulsants for headache prophylaxis. We will use paid, non-reversed Medicaid pharmacy and medical claims data from calendar year 2017, excluding members with Part D, TPL and MaineRX Plus. Will also investigate how many members who require frequent dosing of a triptan are also getting regular botox injections as brophylaxis.

Board Decision: No action needed at this time.

DATA PRESENTATION: 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. We examined 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 identified the reasons for discontinuing naloxone. We also identified how many members have been on buprenorphine for 12 months or more.

We used paid, non-reversed Medicaid pharmacy and medical claims date from CYY 2017 excluding members with Part D, MaineRX and TPL. For the calendar year 2017, there were 81 members who were prescribed buprenorphine for 30 days or more. 29 of those members were switched to buprenorphine alone within 90 days of starting a buprenorphine/naloxone combination product. Only 4 members were on buprenorphine for 12 months or more in 2017. Of the 4 members on buprenorphine the entire calendar year, one member reportedly had a severe allergic reaction to suboxone in 2012, 2 had allergy to suboxone, and one had severe bilateral lower extremity edema. A sampling of 13 the 29 members who switched to buprenorphine alone soon after starting a combination of buprenorphine and naloxone, revealed that 12 were switched due to pregnancy. Only 1 had an intolerance to Naloxone (edema) listed. Although we excluded a pregnancy diagnosis code from the search, we believe a lag in the coding of pregnancy, for various reasons, caused the discrepancy. In summary, it appears that few members were on buprenorphine alone for an issue other than pregnancy. Currently, practice is changing as studies are showing that naloxone is safe in pregnancy, and fewer members should be on buprenorphine alone in the future.

Board Decision: The Board unanimously approved the above recommendation.

HEPATITIS C- REVIEW CLINICAL CRITERIA AND PA FORM

Change Healthcare presented the board with current hepatitis C PA form. With the section highlighted "Documentation in provider notes (**must be submitted**) showing that member has had no abuse of alcohol and drugs for the previous 6 months. **MUST submit** urine drug screen for members with history of abuse of drugs other than alcohol. Counseling **MUST** be provided and documented regarding non-abuse of alcohol and drugs as well as education on how to prevent HCV transmission" in order to review weather to remove this requirement from the PA form.

Board Decision: The Board unanimously approved the removal of the above section on the Hepatitis C PA form.

NEW DRUG REVIEW

Tavalisse® (fostamatinib disodium hexahydrate); **PDL category**- Hematologic Disorder Treatment Agents

Fostamatinib, the active ingredient of Tavalisse®, is a tyrosine kinase inhibitor with demonstrated activity against spleen tyrosine kinase (SYK). The major metabolite of fostamatinib is R406, and this reduces antibody-mediated destruction of platelets. It is indicated for the treatment of thrombocytopenia in adults with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment. Recommended dose to start is at 100mg PO BID. After a month, if the platelet count has not increased to at least 50 X 10^9/L, increase the dose to 150mg PO BID. Use the lowest dose to achieve and maintain a platelet count at least 50 X 10^9/L as necessary to reduce the risk of bleeding. Treatment should be discontinued after 12 weeks of treatment if the platelet count does not increase to a level sufficient to avoid clinically important bleeding. After obtaining baseline assessments: Monitor CBCs (including platelet counts), monthly until a

stable platelet count is achieved. Thereafter, continue to monitor CBCs, including neutrophils, regularly, monitor liver function tests monthly (e.g. ALT, AST, and bilirubin), Monitor blood pressure every 2 weeks until establishment of a stable dose, then monthly thereafter. Dose modifications for the management of specific adverse reactions, such as hypertension, hepatotoxicity, diarrhea, and neutropenia, may be required. The concomitant use of Tavalisse® with strong CYP3A4 inducers is not recommended. It is recommended to monitor for toxicities of Tavalisse® that may require dose reduction when given concurrently with a strong CYP3A4 inhibitor. Monitor for toxicities of CYP3A4 substrates, of BCRP substrates, and of P-gp substrates that may require dose reduction when given concurrently with Tavalisse®. The safety and efficacy of Tavalisse® were assessed in 2 placebo-controlled studies and one open-label extension study. While in one study a significantly larger number of subjects treated with Tavalisse® achieved a stable platelet response as compared with placebo, statistical significance was not seen in the second study.

Recommendation: Tavalisse® be non-preferred.

Clinical Criteria:

- **Tavalisse** is recommended for patients at risk of bleeding when one line of therapy (steroids, IVIG, splenectomy) has failed.

Board Decision: The Board unanimously approved the above recommendation.

Jynarque® (tolvaptan); **PDL category**- Vasopressin Receptor Antagonist

Tolvaptan, the active ingredient of Jynarque®, is a selective vasopressin V2-receptor antagonist, with an affinity for the V2-receptor that is 1.8 times that of native arginine vasopressin (AVP). Tolvaptan affinity for the V2-receptor is 29 times that for the V1a-receptor. In human cyst epithelial cells, tolvaptan inhibited AVP-stimulated in vitro cyst growth and chloride-dependent fluid secretion into cysts. It is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD). It is recommended to perform blood testing for ALT, AST, and bilirubin prior to starting Jynarque®, at 2 and 4 weeks after starting therapy, monthly for 18 months, and every 3 months thereafter. Monitor for concurrent symptoms that may indicate liver injury. Concomitant use of tolvaptan with strong CYP3A inhibitors is contraindicated. Dose reduction of Jynarque® is recommended while taking concomitant moderate CYP3A inhibitors. Jynarque® was shown to slow the rate of decline in renal function in patients at risk of rapidly progressing ADPKD in 2 trials, including the TEMPO 3:4 study that included patients at earlier stages of disease and the REPRISE study that included patients at later stages. Jynarque® is a selective vasopressin V2-receptor antagonist indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD). It is the first and only treatment approved for this indication. Due to the risk of elevations of liver enzymes, Jynarque® will be available only through a restricted distribution program and liver enzymes will need to be monitored.

Recommendation: Jynarque ® be non-preferred.

Clinical Criteria:

- Clinical PA required for appropriate diagnosis
- **DDI: Jynarque**- Concomitant use with strong CYP3A inhibitors is contraindicated. Avoid concomitant use of Jynarque® with OATP1B1/B3 and OAT3 substrates (e.g. statins, bosentan, glyburide, nateglinide, repaglinide, methotrexate, furosemide).

Board Decision: The Board unanimously approved the above recommendation with the change of dividing the category into two subcategories for PDL placement.

Palynziq® (pegvaliase-pqpz**); PDL category- Phenylketonuria (PKU) Treatment Agents- Injectables**

Pegvaliase-pqpz, the active ingredient of Palynziq®, is a phenylalanine-metabolizing enzyme that is composed of recombinant phenylalanine ammonia lyase (rAvPAL) conjugated to N-hydroxysuccinimide (NHS)-methoxypolyethylene glycol (PEG). It is a PEGylated phenylalanine ammonia lyase (PAL) enzyme that converts phenylalanine to ammonia and *trans*-cinnamic acid. It substitutes for the deficient phenylalanine hydroxylase (PAH) enzyme activity in patients with phenylketonuria (PKU) and reduces blood phenylalanine concentrations. Treatment of adults with PKU resulted in the reduction of blood phenylalanine concentrations from pre-treatment baseline. It is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management. *Study 301* was an open-label, randomized, multicenter study that included adults with PKU to assess the safety and tolerability of self-administered Palynziq® in an induction/titration/maintenance regimen with a target maintenance dose of 20mg SC QD or 40mg SC QD. Study 302 was an efficacy trial that included 152 patients from Study 301 and 12 patients from other Palynziq® clinical trials. In the double-blind, placebo-controlled, randomized withdrawal period, patients were randomized to either continue their maintenance Palynziq® dose or to receive matching placebo for a total of 8 weeks.

Recommendation: Palynziq® be non-preferred Add new category Phenylketonuria (PKU) Treatment Agents with two sub-categories injectables and oral. Add Kuvan to the non-preferred side of the PDL under the oral sub-category.

Clinical Criteria:

- Palynziq is not to be used in combination with Kuvan.
- Palynziq: For the treatment of patients ≥ 18 years of age.

Board Decision: The Board unanimously approved the above recommendation.

Retacrit® (epoetin alfa-epbx); **PDL category**- Erythropoietin

Epoetin alfa-epbx is an erythropoiesis-stimulating glycoprotein manufactured by recombinant DNA technology. Epoetin alfa products stimulate erythropoiesis by the same mechanism as endogenous erythropoietin. Epoetin alfa increases the reticulocyte count within 10 days of starting, followed by increases in the red blood cell (RBC) count, hemoglobin, and hematocrit, usually within 2 to 6 weeks. It is indicated for the following: Anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC) transfusion, Anemia due to zidovudine in patients with HIV-infection, due to zidovudine administered at ≤4,200mg/week in patients with HIV-infection with endogenous serum erythropoietin levels of ≤500 mUnits/mL, Anemia due to chemotherapy in patients with cancer, with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of 2 additional months of planned chemotherapy, To reduce the need for allogeneic RBC transfusions among patients with perioperative hemoglobin >10 to ≤13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery. It is not indicated for patients who are willing to donate autologous blood pre-operatively. Retacrit® has not been

shown to improve quality of life, fatigue, or patient well-being. Retacrit® was FDA approved as a biosimilar to Epogen®/Procrit®, but has not been shown to be interchangeable with Epogen®/Procrit®. It is the first FDA approved epoetin alfa biosimilar. Per the FDA, "a biosimilar is a biological product that is approved based on data showing that it is highly similar to a biological product already approved by the FDA (reference product) and has no clinically meaningful differences in terms of safety, purity, and potency (i.e. safety and effectiveness) from the reference product, in addition to meeting other criteria specified by law.

Recommendation: Retacrit® be non-preferred.

Clinical Criteria: Non-Preferred drugs must be tried and failed in step-order, 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.

Symtuza® (darunavir, cobicstat, emtricitabine & tenofovir alafenamide); **PDL category**- Antiretrovirals

Symtuza® is a fixed-dose combination tablet containing darunavir (an inhibitor of the HIV-1 protease), cobicistat (inhibitor of CYP3A family), emtricitabine (an HIV nucleoside analog reverse transcriptase inhibitor or HIV NRTI), and tenofovir alafenamide (an HIV NRTI and a prodrug converted to tenofovir). All agents except for cobicistat are antiretroviral agents for the HIV-1 virus. Cobicistat has no antiretroviral activity, but rather is a selective inhibitor of the CYP3A subfamily and thus enhances the systemic exposure of CYP3A substrates (darunavir). It is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults: Who have no prior antiretroviral treatment history OR Who are virologically suppressed (HIV-1 RNA <50 copies/ml) on a stable antiretroviral regimen for at least 6 months and have no known substitutions associated with resistance to darunavir or tenofovir. The efficacy of Symtuza® in HIV-1 adults with no prior antiretroviral treatment history was assessed in a phase 3 trial that included adults randomized to Symtuza (N=362) or a combination of Prezcobix® (fixed-dose combination of darunavir and cobicistat) and fixed-dose combination of emtricitabine (FTC) and tenofovir disoproxil fumarate. There is no evidence that Symtuza® is safer or more effective than the currently available, more cost-effective medications including taking the same ingredients using different combination pills.

Recommendation: Symtuza® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Lucemyra® (lofexidine); **PDL category**- Opioid Withdrawal Agents

Lofexidine, the active ingredient of Lucemyra®, is a central alpha-2 adrenergic agonist that binds to receptors on adrenergic neurons. This reduces the release of norepinephrine and decreases sympathetic tone. It is indicated for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults. There were 2 randomized, double-blind placebo-controlled studies to assess the safety and efficacy of Lucemyra®. In clinical studies, it was found to significantly reduce the SOWS-Gossop total score as compared with placebo, and a significantly larger number of subjects completed treatment with Lucemyra® as

compared with placebo. There is no evidence that Lucemyra® is more effective than the currently available, more cost-effective medications; however, there is some evidence that it may cause less hypotension and other side effects compared to clonidine, although a Cochrane review graded this evidence as "low quality."

Recommendation: Lucemyra® be non-preferred.

Clinical Criteria:

- Clinical PA for appropriate approved use and patient has documented contraindication to clonidine.

Board Decision: The Board unanimously approved the above recommendation.

Fulphila® (pegfilgrastim-jmdb); **PDL category**- Granulocyte CSF

Pegfilgrastim-jmdb is a conjugate of methionyl human granulocyte-colony stimulating factor (G-CSF) and monomethoxypolyethylene glycol. Pegfilgrastim products are CSFs that act on hematopoietic cells by binding to specific cell surface receptors, thus stimulating proliferation, differentiation, commitment, and end-cell functional activation. It is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. It is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation. It is contraindicated in patients with a history of serious allergic reactions to pegfilgrastim products or filgrastim products. Pegfilgrastim was assessed in 3 randomized, double-blind controlled studies that included patients with cancer receiving myelosuppressive chemotherapy. Fulphila® is a biosimilar to Neulasta® but is not approved as an interchangeable product. Per the package insert, biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. There is no evidence at this time to support that Fulphila® is safer or more effective than the currently available, more cost-effective medications.

Recommendation: Fulphila® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Bonjesta® (doxylamine succinate and pyridoxine HCL**); PDL category- Antiemetics-Anticholingergics/Dopaminergic**

Bonjesta® is a combination extended-release product that contains an enteric-coated core containing 10mg doxylamine and 10mg pyridoxine, and an immediate-release coating of 10mg of doxylamine and 10mg pyridoxine. The active ingredients include the antihistamine doxylamine and the vitamin B6 analog pyridoxine. The exact mechanism of action for use as an anti-emetic in pregnant women is not known. It is indicated for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management. Use has not been studied in women with hyperemesis gravidarum. There is no pregnancy category for this product; however, the risk summary indicates that Bonjesta® is intended for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management. No increased risk for congenital malformations has been reported in studies in pregnant women. The safety and efficacy of use in children under 18 years of age have not been established. The drug combination of doxylamine and pyridoxine was originally marketed in the US under the brand name Bendectin® between

1956 and 1983; however, it was removed from the market due to concerns about birth defects. Nevertheless, unsupported concerns led to the continued use of the single-entity individual ingredients, and now to the FDA approval of Bonjesta®. There have been no safety and efficacy trials conducted with Bonjesta®. In a 2018 practice bulletin by the American College of Obstetricians and Gynecologists, pyridoxine plus doxylamine is recommended as a pharmacologic option for the treatment of nausea and vomiting of pregnancy if symptoms persist after first line therapy of non-pharmacologic options (e.g. acupressure with wrist bands). If symptoms persist with pyridoxine plus doxylamine, then other agents can be added, such as prochlorperazine or promethazine. There is no evidence at this time to support that Bonjesta® is safer or more effective than the currently available, more cost-effective medications or the combination of the individual ingredients.

Recommendation: Bonjesta® be non-preferred.

Clinical Criteria:

- DDI: Concomitant use of MAOIs and Bonjesta® is contraindicated.

Board Decision: The Board unanimously approved the above recommendation.

Olumiant® (baricitinib); **PDL category**- Rheumatoid Arthritis

Baricitinib, the active ingredient of Olumiant®, is a Janus Kinase (JAK) Inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membranes to influence cellular processes of hematopoiesis and immune cell function. It is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies. Use in combination with other JAK inhibitors, biologic disease-modifying antirheumatic drugs (DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended. The safety and efficacy of Olumiant® were assessed in 2 dose-ranging and 4 confirmatory phase 3 trials. There is some evidence at this time, in a phase 3 study, that may suggest baricitinib 4mg is more effective than adalimumab; however, Olumiant® is only FDA approved for 2mg. In addition, there is no evidence to support that Olumiant® is safer or more effective than the other currently available, more cost-effective medications.

Recommendation: Olumiant ® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

FDA warns about increased risk of cancer relapse with long-term use of azithromycin (Zithromax, Zmax) antibiotic after donor stem cell transplant
https://www.fda.gov/Drugs/DrugSafety/ucm614085.htm

FDA reinforces safety information about serious low blood sugar levels and mental health side effects with fluoroquinolone antibiotics; requires label changes
https://www.fda.gov/Drugs/DrugSafety/ucm611032.htm

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **October 09, 2018** 5:30pm –8:30pm at the Augusta Armory.