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: 09/18/20
RE: Maine DUR Board **Meeting** minutes from September 08, 2020

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		
Erin Ackley, PharmD.			X
Corinn Martineau, PharmD.	X		
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare	X		
Laureen Biczak, DO, Change Healthcare	X		
Jill Kingsbury, MaineCare Pharmacy Director	X		

Guests of the Board: Ed Bosshart, PharmD

CALL TO ORDER: 5:30PM

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

PUBLIC COMMENTS

Sarah Hnath and Tim Wardell from Abbvie: Highlighted the attributes of Durysta and Oriahnn.
Matt Clark from Zogenix: Highlighted the attributes of Fintepla.
Elizabeth Lubelczyk and Angelo Deluca from Eli Lilly: Highlighted the attributes of Lyumjev and Retevmo.
Ken Smith from Genetech: Highlighted the attributes of Phesgo.

OLD BUSINESS

DUR MINUTES

The June DUR meeting minutes were accepted.

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE

Welcome Jenny Patterson as the new Directory of Policy at MaineCare. She is a graduated of Harvard and brings over 20 years of experience with state government.

REVISED CLINICAL CRITERIA/PREFERRED REVIEW

Biosimilars:
Avsola® **PDL category-** Rheumatoid Arthritis

Recommendation: Add Avsola to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Prior Authorization (PA) Form:
Change Healthcare explained the changes and clinical rational on the updated Antibacterial Antibiotic PA Form.

Recommendation: Update PA form

Board Decision: The Board unanimously approved the above recommendation.

NEW BUSINESS

DATA PRESENTATION: PREP HIV THERAPY PRESCRIBING RATES

Pre-exposure prophylaxis (PrEP) with antiretroviral drugs has become standard of care for those at high risk of contracting HIV. People considered at high risk include those who have sex with HIV-infected partners, those who have recent histories of STDs and/or high numbers of sex partners, those who are commercial sex workers and IV drug users, especially those whose injecting partners are HIV positive. Eligible patients should have a documented negative HIV test prior to starting PrEP and have no symptoms of acute HIV infection. Additionally, they should be tested for hepatitis B and appropriately vaccinated, as PrEP treatment can worsen hepatitis B infections. Renal function should be tested and be normal and there should be documentation of other drugs taken, as there are significant drug/drug interactions with some antiretroviral medications. Once the decision is made to start PrEP therapy, it is necessary to educate the patient about the monitoring that will need to be adhered to in order to continue therapy. This includes an HIV test every 3 months, medication adherence counseling, side effect assessment and STD symptom assessment. Renal function should be assessed at 3 months, and if stable, every 6 months thereafter. Women should have a pregnancy test every 3 months.

The recommended treatment for PrEP therapy is Truvada, a combination of tenofovir disoproxil fumarate (a nucleotide reverse transcriptase inhibitor (NRTI)) and emtricitabine (also an NRTI) integrase inhibitor), or Descovy (tenofovir alafenamide (NRTI) and emtricitabine), if the patient has renal insufficiency. We used paid, non-reversed Medicaid pharmacy and medical claims dated from October 2018 through calendar year 2019 excluding members with Part D, MaineRX and TPL. We identified members getting either Truvada or Descovy alone and examined medical claims to see if the guidelines for monitoring had been followed, including pre-prescribing HIV and Hep B testing, documentation of recent creatinine or BMP, as well as pregnancy testing in women. Additionally, we looked to see if HIV

testing, creatinine and pregnancy testing was done at 3 months intervals, as recommended in guidelines.

Recommendation: There was generally poor adherence to monitoring members on PrEP therapy. It might be helpful to reach out to the providers of members who had no laboratory monitoring to see whether this testing was actually performed and not captured in our analysis or what the barriers to compliance with guidelines was and determine plan of action based on those findings. Possible interventions could be to remind prescribers of PrEP therapy in real time of the need for monitoring, mailing a general reminder to all prescribers of PrEP therapy of the monitoring guidelines. Given the results, before moving forward Change Healthcare recommends that we audit 5-8 charts to confirm that the data is correct.

Board Decision: The Board unanimously approved the above recommendation.

INTRODUCE: CHANTIX USE

The benefits of smoking cessation are obvious. While some people quit on their own, either by tapering or going "cold turkey", many will require the aid of counseling, medications or both. It has been demonstrated that of those who use medication, long-term abstinence often requires counseling in addition to medication. Luckily, several medications have been used successfully, including nicotine replacement products (short- and long-acting), bupropion and varenicline (Chantix). While initially there was concern that Chantix was associated with neuropsychiatric side effects, including risk of suicide, a recent, large study (EAGLES trial of 8000 smokers randomized to NRT, bupropion or varenicline or placebo) showed that the risk was equal among treatments and a black box warning was removed. Many who take Chantix have already tried nicotine replacement products unsuccessfully. While Chantix is meant to be used alone, there has been some success in adding short-acting NRTs in those who continue to experience withdrawal symptoms. In those who have successfully quit at 12 weeks, some may benefit from an additional 12 weeks of therapy to prevent relapse.

We will use paid, non-reversed Medicaid pharmacy and medical claims date from calendar year 2019 excluding members with Part D, MaineRX and TPL. We will look at all member who were prescribed Chantix and evaluation the number of monthly prescriptions dispensed per member. Additionally, we will see which members were also simultaneously prescribed a short acting nicotine replacement product (gum, lozenges, inhaler, nasal spray). Will look to see if there were any members taking either bupropion or the long acting nicotine patches, which is not common practice or recommended.

Board Decision: No action needed at this time.

NEW DRUG REVIEW

Ayvakit® (avapritinib; **PDL category-** Cancer

Avapritinib, the active ingredient of Ayvakit®, is a tyrosine kinase inhibitor that targets platelet-derived growth factor receptor alpha (PDGFRA) and PDGFRA D842 mutants as well as multiple KIT exon 11, 11/17, and 17 mutants. It is indicated for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations. The safety and efficacy of Ayvakit® were assessed in a single-

arm, multicenter, open-label study that included patients required to have a confirmed diagnosis of GIST and an ECOG performance status of 0 to 2. The trial initially enrolled patients at a starting dose of 400mg, which was later reduced to the recommended dose of 300mg due to toxicity. As there was no apparent difference in overall response rate (ORR) between patients who received 300mg daily compared to those who received 400mg daily, these patients were pooled for the efficacy assessment. The main outcome assessed was ORR based on disease assessment by independent radiological review using modified RECIST v1.1 criterion, in which lymph nodes and bone lesions were not target lesions and progressively growing new tumor nodules within a pre-existing tumor mass was progression. Duration of response (DOR) was also assessed. An FDA-approved test for the detection of exon 18 mutations is not currently available. In a single-arm study, overall response rate was seen in 84% of patients. It is recommended that Ayvakit® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use, as well as prior trials of preferred therapies.

Recommendation: Ayvakit® to non-preferred.

Clinical criteria: All non-preferred: A clinical PA is required to confirm appropriate clinical indication for the individual drug request. Specific to each drug all age, clinical testing requirements, previous step therapies, adjunctive drug therapy requirements, and response without disease progression will be also be evaluated for clinical appropriateness. The standard for the appropriate indication will include the FDA label as well as current NCCN guidelines.

Board Decision: The Board unanimously approved the above recommendation.

Bynfezia® (octreotide); **PDL category-** Somatostatic Agents

Octreotide, the active ingredient of Bynfezia® Pen, exerts pharmacologic actions similar to the natural hormone, somatostatin. Octreotide is an even more potent inhibitor of growth hormone, glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses luteinizing hormone (LH) response to gonadotropin releasing hormone (GnRH), decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide. With these actions, octreotide has been used to treat the symptoms associated with metastatic carcinoid tumors (flushing and diarrhea), and VIP secreting adenomas (watery diarrhea). It is indicated for: Acromegaly: To reduce blood levels of growth hormone (GH) and insulin-like growth factor 1 (IGF-1) [somatomedin C] in adults with acromegaly who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses, Carcinoid Tumors: For the treatment of adults with severe diarrhea and flushing episodes associated with metastatic carcinoid tumors, Vasoactive Intestinal Peptide Tumors (VIPomas): For the treatment of adults with the profuse watery diarrhea associated with VIP-secreting tumors. In patients with acromegaly, the effect of Bynfezia® Pen on improvement in clinical signs and symptoms, reduction in tumor size, and rate of growth has not been determined. In patients with carcinoid syndrome and VIPomas, the effect of Bynfezia® Pen on the tumor size, rate of growth, and development of metastases has not been determined. There is no clinical trials section in the Bynfezia® Pen prescribing information. Octreotide injection, under brand name Sandostatin,® has the same indications as Bynfezia® Pen, has been available for numerous years, and has been found to be safe and effective. Sandostatin® can be administered intravenously or subcutaneously. Bynfezia® Pen is for subcutaneous use; it should be stored in the refrigerator but after the first use it can be stored at room temperature. The multi-dose Bynfezia® Pen should be discarded 28 days after first use. Bynfezia® Pen

allows for a different dosage form for patients that can be stored at room temperature after the first use and injected subcutaneously by the patient.

Recommendation: Bynfezia® to non-preferred.

Clinical Criteria:

- Move Octreotide to step 7.
- All other drug in category step 8.
- Non-preferred products must be used in specified step order.

Board Decision: The Board unanimously approved the above recommendation.

Durysta® (bimatoprost implant); **PDL category**- OP- Prostaglandins

Bimatoprost, the active ingredient of Durysta®, is a prostaglandin analog. It is a synthetic structural analog of prostaglandin with ocular hypotensive activity. It is believed to lower intraocular pressure in humans by increasing outflow of aqueous humor through both the trabecular meshwork (conventional) and uveoscleral routes (unconventional). Elevated intraocular pressure presents a major risk factor for glaucomatous field loss. The higher the level of intraocular pressure, the greater the likelihood of optic nerve damage and visual field loss. It is indicated for the reduction of intraocular pressure (IOP) in patients with open angle glaucoma (OAG) or ocular hypertension (OHT). The efficacy of Durysta® was assessed in two multicenter, randomized, parallel-group, controlled studies of 20 months in duration. Durysta® implant was compared to twice daily topical timolol 0.5% drops in patients with OAG or OHT. Results suggested that Durysta® demonstrated an IOP reduction of about 5-8mmHg in patients with a mean baseline IOP of 24.5mmHg. In two clinical trials, Durysta® was found to have similar reduction in IOP as compared with daily timolol ophthalmic drops. There is no evidence at this time to support that Durysta® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Durysta® to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Fensolvi® (leuprolide acetate); **PDL category-** Central Precocious Puberty Agents

Leuprolide acetate, the active ingredient of Fensolvi®, is a gonadotropin releasing hormone (GnRH) agonist and acts as a potent inhibitor of gonadotropin secretion (luteinizing hormone [LH] and follicle stimulating hormone [FSH]) when given continuously in therapeutic doses. After an initial stimulation of GnRH receptors, chronic administration of leuprolide results in downregulation of GnRH receptors, reduction in release of LH, FSH, and consequent suppression of ovarian and testicular production of estradiol and testosterone respectively. This inhibitory effect is reversible upon discontinuation of drug therapy. It is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP). The efficacy of Fensolvi® was assessed in an uncontrolled, open-label, single-arm study that included pediatric patients (62 females and 2 males, naïve to previous GnRH agonist treatment) with CPP who received at least one dose of Fensolvi® at a dosing interval of 24 weeks and who were observed for 12 months. It is the first and only six-month subcutaneously administered leuprolide, and it demonstrated clinical efficacy in a single-arm, open-label study with suppression of peak stimulated LH concentrations. Fensolvi® utilizes the ATRIGEL Delivery system, which is a polymeric (non-gelatin

containing) delivery system consisting of a biodegradable poly(DL-lactide-co-glycolide) (PLG) polymer formulation dissolved in the biocompatible solvent, N-methyl-2-pyrrolidone (NMP), and leuprolide is released in a sustained manner over a six-month dosing cycle. There is no evidence at this time to support that Fensolvi® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Fensolvi® be non-preferred.

Clinical Criteria:

- Add new subcategory Central Precocious Puberty Agents.
- Add for pediatric patients 2 years of age and older with central precocious puberty (CPP).

Board Decision: The Board unanimously approved the above recommendation.

Fintepla® (fenfluramine); **PDL category**- Anticonvulsants

The exact mechanism of action of fenfluramine, the active ingredient of Fintepla®, is not known. Fenfluramine and its metabolite, norfenfluramine, increase extracellular levels of serotonin through interaction with serotonin transporter proteins, and exhibit agonist activity at serotonin 5HT-2 receptors. It is indicated for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older. The safety and efficacy of Fintepla® for the treatment of seizures associated with Dravet syndrome in patients 2 to 18 years of age were assessed in two randomized, double-blind, placebo-controlled studies. In both studies, patients had a clinical diagnosis of Dravet syndrome and were inadequately controlled on at least one antiepileptic drug (AED) or other antiseizure treatment, including vagal nerve stimulation or a ketogenic diet. In clinical trials compared with placebo, all doses of Fintepla® assessed statistically significantly reduced convulsive seizure frequency per 28 days. Comparator studies with active treatments were not found.

Recommendation: Fintepla® be non-preferred.

Clinical Criteria:

- Add for seizures associated with Dravet syndrome in patients 2 years of age and older.

Board Decision: The Board unanimously approved the above recommendation.

Kynmobi® (apomorphine HCL); **PDL category**- Parkinson's- Dopaminergics/Carbidopa/Levodopa

Apomorphine, the active ingredient of Kynmobi®, is a non-ergoline dopamine agonist with high in vitro binding affinity for the dopamine D4 receptor, and moderate affinity for the dopamine D2, D3, and D5 as well as adrenergic α1D, α2B, α2C receptors. The exact mechanism of action for its approved indication is not known, although it is believed to be due to stimulation of post-synaptic dopamine D2-type receptors within the caudate-putamen in the brain. It is indicated for the acute, intermittent treatment of "off" episodes in patients with Parkinson's disease (PD). The safety and efficacy of Kynmobi® for the acute, intermittent treatment of 'off' episodes in patients with Parkinson's disease were established in one randomized, double-blind, placebo-control, parallel-group study. The study included adults with a mean duration of Parkinson's disease of about 9 years (range 2 to 22 years) who were Hoehn and Yahr Stage III or less in the 'on' state and who were all receiving concomitant levodopa with a stable dose for at least 4

years before screening. In a clinical trial compared with placebo, Kynmobi® significantly improved (i.e. reduction in score) the change in the MDS-UPDRS III from pre-dose to 30 minutes post-dose at the 12-week visit. Apomorphine has been available under the brand name Apokyn® for numerous years as a subcutaneous injection dosage form.

Recommendation: Kynmobi® 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.

Lyumjev® (insulin lispro- aabc); **PDL category**- Diabetic- Insulins

Insulin lispro-aabc, the active ingredient of Lyumjev®, is a rapid-acting human insulin analog produced by recombinant DNA technology. Insulin lispro-aabc differs from human insulin in that the amino acid proline at position B28 is replaced by lysine and the lysine in position B29 is replaced by proline. The primary activity of Lyumjev® is the regulation of glucose metabolism. Insulins exert their specific action through binding to insulin receptors and lowers glucose by stimulating peripheral glucose uptake by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulins inhibit lipolysis and proteolysis and enhance protein synthesis. It is indicated for to improve glycemic control in adults with diabetes mellitus (DM). The safety and efficacy of Lyumjev® were assessed in two randomized, active-controlled trials of 26 weeks in duration that included adults with type 1 DM or type 2 DM. In the two clinical trials, PRONTO T1D3 and PRONTO T2D2, Lyumjev® was non-inferior to Humalog® for HbA1c reduction (primary outcome). However, per the full-text studies, mealtime rapid-acting lispro-aabc was superior to lispro in reducing 1- and 2- hour postprandial glucose excursions during the meal test in PRONTO T1D (estimated treatment difference -1.55mmol/L at 1 hour and -1.73 mmol/L at 2 hours; both $p<0.001$) and PRONTO T2D (estimated treatment differences -0.66mmol/L at 1 hour and -0.96mmol/L at 2 hours; $p<0.05$). There is no evidence at this time to support that Lyumjev® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Lyumjev® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Nexlizet® (bempedoic acid and ezetimibe); **PDL category**- Cholesterol- HMG-CoA + Absorb Inhibitors, Less Potent Drugs/ Combos

Nexlizet® contains bempedoic acid and ezetimibe. Bempedoic acid is an adenosine triphosphate-citrate lyase (ACL) inhibitor that lowers LDL-C by inhibition of cholesterol synthesis in the liver. ACL is an enzyme upstream of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase in the cholesterol biosynthesis pathway. Bempedoic acid and its active metabolite (ESP15228) require coenzyme A (CoA) activation by very long-chain acyl-CoA synthetase 1 (ACSVL1) to ETC-1002-CoA and ESP15228-CoA,

respectively. ACSVL1 is expressed mainly in the liver. Inhibition of ACL by ETC-1002-CoA results in decreased cholesterol synthesis in the liver and lowers LDL-C in blood via upregulation of low-density lipoprotein receptors. Ezetimibe reduces blood cholesterol by inhibiting the absorption of cholesterol by the small intestine. The molecular target of ezetimibe has been shown to be the sterol transporter Niemann-Pick C1-Like 1 (NPC1L1), which is involved in the intestinal uptake of cholesterol and phytosterols. Ezetimibe localizes at the brush border of the small intestine and inhibits the absorption of cholesterol, leading to a decrease in the delivery of intestinal cholesterol to the liver. This causes a reduction of hepatic cholesterol stores and an increase in LDL receptors, resulting in clearance of cholesterol from the blood. It is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C. The effect of Nexlizet® on cardiovascular morbidity and mortality has not been determined. The safety and efficacy of Nexlizet® were assessed in a multicenter, randomized, double-blind, placebo-controlled parallel group study that included adults with heterozygous familial hypercholesterolemia (HeFH), established atherosclerotic cardiovascular disease (ASCVD), or multiple risk factors for cardiovascular disease on maximally tolerated statins. The efficacy of Nexlizet® in patients with multiple risk factors for cardiovascular disease has not been established. A clinical study assessed the percent change from baseline to week 12 in LDL-C with Nexlizet® as compared with placebo for the primary endpoint, and the difference was highly significant in favor of Nexlizet®. In the 2019 full-text study by Ballantyne et al2, bempedoic acid plus ezetimibe fixed-dose combination was significantly more effective than either individual agent for LDL-C reduction. There is some evidence to suggest that Nexlizet® may be more effective than its individual ingredients for lowering cholesterol; however, there is no evidence at this time to support that Nexlizet® is safer or more effective than the currently preferred, more cost-effective medications.

Recommendation: Nexlizet® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Phesgo® (pertuzumab, trastuzumab, and hyaluronidase-zzxf); **PDL category**- Cancer

Phesgo® is a combination product that contains pertuzumab (a recombinant humanized monoclonal antibody that targets the extracellular dimerization domain (Subdomain II) of the human epidermal growth factor receptor 2 protein (HER2)), trastuzumab (a humanized IgG1 kappa monoclonal antibody that selectively binds with high affinity to the extracellular domain of the HER2), and hyaluronidase, recombinant human (an endoglycosidase used to increase the dispersion and absorption of co-administered drugs when given subcutaneously). Pertuzumab blocks ligand-dependent heterodimerization of HER2 with other HER family members. As a result, pertuzumab inhibits ligand-initiated intracellular signaling through two major signaling pathways, including mitogen-activated protein (MAP) kinase and phosphoinositide 3-kinase (PI3K). Inhibition of these signaling pathways can result in cell growth arrest and apoptosis, respectively. Trastuzumab inhibits the ligand independent, HER2 mediated cell proliferation and PI3K signaling pathway in human tumor cells that overexpress HER2. Both pertuzumab and trastuzumab-mediated antibody-dependent cell-mediated toxicity have been shown to be preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2. Hyaluronan is a polysaccharide found in the extracellular matrix of the subcutaneous tissue. It is depolymerized by the naturally occurring enzyme hyaluronidase. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan. In the doses administered, hyaluronidase in Phesgo® acts transiently and locally. The effects of hyaluronidase are

reversible and permeability of the subcutaneous tissue is restored within 24 to 48 hours. It is indicated for the Early Breast Cancer (EBC): for use in combination with chemotherapy for

- The neoadjuvant treatment of adults with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2cm in diameter or node positive) as part of a complete treatment regimen for EBC
- The adjuvant treatment of adults with HER2-positive early breast cancer at high risk of recurrence

Metastatic Breast Cancer (MBC): for use in combination with docetaxel for the treatment of adults with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease. The efficacy of Phesgo® for use in combination with chemotherapy has been established for the treatment of patients with HER2-positive early breast cancer (EBC). Use of Phesgo® for this indication is supported by evidence from adequate and well-controlled studies conducted with IV pertuzumab and IV trastuzumab administered in combination with chemotherapy in adults with HER2-overexpressing EBC and additional pharmacokinetic and safety data that demonstrated comparable pharmacokinetics and safety profiles between Phesgo® and IV pertuzumab and IV trastuzumab in the FeDeriCa Study. In a non-inferiority study, the pertuzumab cycle 7 Ctrough demonstrated non-inferiority of pertuzumab within Phesgo® to IV pertuzumab. Similar results were seen with trastuzumab within Phesgo® to IV trastuzumab. Do not substitute Phesgo® for or with pertuzumab, trastuzumab, ado-trastuzumab emtansine, or fam-trastuzumab deruxtecan.

Recommendation: Phesgo® to be non-preferred.

Clinical criteria: All non-preferred: A clinical PA is required to confirm appropriate clinical indication for the individual drug request. Specific to each drug all age, clinical testing requirements, previous step therapies, adjunctive drug therapy requirements, and response without disease progression will be also be evaluated for clinical appropriateness. The standard for the appropriate indication will include the FDA label as well as current NCCN guidelines.

Board Decision: The Board unanimously approved the above recommendation.

Oriahnn® (elagolix, estradiol, norethindrone); **PDL category**- Endometriosis/Uterine Fibroids

Oriahnn® is a combination of elagolix (a gonadotropin-releasing hormone [GnRH] receptor antagonist), estradiol (an estrogen), and norethindrone acetate (a progestin). Elagolix is a GnRH receptor antagonist that inhibits endogenous GnRH signaling by binding competitively to GnRH receptors in the pituitary gland. Administration of elagolix results in dose-dependent suppression of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to decreased blood concentrations of the ovarian sex hormones estradiol and progesterone and reduces bleeding associated with uterine fibroids. Estradiol (E2) acts by binding to nuclear receptors that are expressed in estrogen-responsive tissues. The addition of exogenous estradiol may reduce the increase in bone resorption and resultant bone loss that can occur due to a decrease in circulating estrogen from elagolix alone. Norethindrone acetate (NETA) acts by binding to nuclear receptors that are expressed in progesterone-responsive tissues. As a component of Oriahnn®, NETA may protect the uterus from the potential adverse endometrial effects of unopposed estrogen. It is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of Oriahnn® should be limited to 24 months due to the risk of continued bone loss, which may not be reversible. The efficacy of Oriahnn® in the management of heavy menstrual bleeding (HMB) associated with uterine fibroids was assessed in two randomized, double-blind, placebo-controlled studies. In two clinical trials, significantly more women treated with

Oriahnn® were responders for the primary outcome (menstrual blood loss volume less than 80ml at the final month and ≥50% reduction in menstrual blood loss volume from baseline to the final month). The NNT for the primary outcome (calculated by CHC) was 2 in both study 1 and 2.

Recommendation: Oriahnn ® be non-preferred.

Clinical criteria:

- Update subcategory to Endometrosis/Uterine Fibroids- Oral.
- Add limited to 24 months due to the risk of continued bone loss, which may not be reversible.

Board Decision: The Board unanimously approved the above recommendation.

Ortikos® (budesonide); **PDL category**- Glucocorticoids/Mineralocorticiods

Budesonide, the active ingredient of Ortikos®, is a synthetic corticosteroid. It is an anti-inflammatory corticosteroid and has a high glucocorticoid effect and a weak mineralocorticoid effect. It is indicated for the treatment of mild to moderate active Crohn's disease involving the ileum and/or the ascending colon in patients 8 years of age and older and Maintenance of clinical remission of mild to moderate Crohn's disease involving the ileum and/or the ascending colon for up to 3 months in adults. The safety and efficacy of Ortikos® have been established based on adequate and well-controlled adult studies of another oral budesonide product in patients with Crohn's disease. The clinical studies included in the Ortikos® prescribing information are the same as in the Entocort® EC prescribing information. Entocort® EC is available as a 3mg delayed release capsule and has the same indications as Ortikos®. Entocort® EC has been available for numerous years and has been found to be safe and effective, while now having an available generic. Entocort® EC capsules can be opened and mixed in with applesauce for administration in those unable to swallow capsules. There was no information found in the prescribing information for Ortikos® indicating that the capsules could be opened and mixed with applesauce. The safety and efficacy of Ortikos® have been established based on adequate and well-controlled adult studies of another oral budesonide product (Entocort® EC) in patients with Crohn's disease. Entocort® EC is available only as a 3mg delayed release capsule and can be opened and mixed in with applesauce for administration in those unable to swallow capsules whole. Ortikos® hard gelatin capsules are available as 6mg and 9mg.

Recommendation: Ortikos® Pen be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Qinlock® (ripretinib); **PDL category**- Cancer

Ripretinib, the active ingredient of Qinlock®, is a tyrosine kinase inhibitor that inhibits KIT proto-oncogene receptor tyrosine kinase (KIT) and platelet derived growth factor receptor A (PDGFRA) kinase, including wild type, primary, and secondary mutations. It is indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib. The safety and efficacy of Qinlock® were assessed in a multicenter, randomized, double-blind, placebo-controlled trial that included patients who had unresectable, locally advanced or metastatic GIST and who had received prior treatment with imatinib, sunitinib, and regorafenib. In a placebo-controlled trial, Qinlock® significantly prolonged progression-free survival and

overall survival in a patient population with unresectable, locally advanced or metastatic GIST who had received prior treatment with imatinib, sunitinib, and regorafenib.

Recommendation: Qinlock® be non-preferred.

Clinical criteria: All non-preferred: A clinical PA is required to confirm appropriate clinical indication for the individual drug request. Specific to each drug all age, clinical testing requirements, previous step therapies, adjunctive drug therapy requirements, and response without disease progression will be also be evaluated for clinical appropriateness. The standard for the appropriate indication will include the FDA label as well as current NCCN guidelines.

Board Decision: The Board unanimously approved the above recommendation.

Retevmo® (selpercatinib); **PDL category**- Cancer

Selpercatinib, the active ingredient of Retevmo®, is a kinase inhibitor that inhibits wild type RET and multiple mutated RET isoforms as well as VEGFR1 and VEGFR3. It is indicated for the treatment of

- Adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC).
- Adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy.
- Adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials. The safety and efficacy of Retevmo® were assessed in patients with advanced RET fusion-positive NSCLC in a multicenter, open-label multicohort study that enrolled patients with advanced or metastatic RET fusion-positive NSCLC who had progressed on platinum-based chemotherapy and patients with advanced or metastatic NSCLC without prior systemic therapy in separate cohorts. Retevmo is a kinase inhibitor indicated for metastatic RET fusion-positive non-small cell lung cancer, RET mutant medullary thyroid cancer, and RET fusion-positive thyroid cancer. Retevmo® can cause concentration-dependent QT interval prolongation. In the various studies, there has been an overall response rate of at least 64%.

Recommendation: Retevmo® to be non-preferred.

Clinical criteria: All non-preferred: A clinical PA is required to confirm appropriate clinical indication for the individual drug request. Specific to each drug all age, clinical testing requirements, previous step therapies, adjunctive drug therapy requirements, and response without disease progression will be also be evaluated for clinical appropriateness. The standard for the appropriate indication will include the FDA label as well as current NCCN guidelines.

Board Decision: The Board unanimously approved the above recommendation.

Rukobia® (fostemsavir tromethamine, extended release); **PDL category**- Antiretrovirals

Fostemsavir tromethamine, the active ingredient of Rukobia®, is a prodrug of temsavir, an HIV-1 gp120-directed attachment inhibitor. Fostemsavir is a prodrug without significant biochemical or antiviral activity that is hydrolyzed to the active moiety, temsavir. Temsavir is an antiretroviral agent that binds directly to the gp120 subunit within the HIV-1 envelope glycoprotein gp160 and selectively inhibits the interaction between the virus and cellular CD4 receptors, thus preventing attachment. In addition, temsavir can inhibit gp120-dependent post-attachment steps required for viral entry into host cells. It is indicated 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 due to resistance, intolerance, or safety considerations. The efficacy of Rukobia® in heavily treatment-experienced adults with HIV-1 infection was based on 96-week data from a phase 3, partially randomized, international, double-blind, placebo-controlled trial (BRIGHTE) that included heavily treatment-experienced subjects with multi-class HIV-1 resistance. In a double-blind, randomized cohort, Rukobia® demonstrated superiority over placebo for the primary endpoint of adjusted mean decline in HIV-1 RNA from day 1 to day 8 in a population infected with HIV-1 and current regimen failure. Rukobia® should be used with caution in patients with a history of QTc interval prolongation, when co-administered with a drug with a known risk of Torsade de Pointes, or in patients with relevant pre-existing cardiac disease.

Recommendation: Rukobia® to be preferred.

Clinical criteria:

- Add Clinical PA required.

Board Decision: The Board unanimously approved the above recommendation.

Tabrecta® (capmatinib); **PDL category**- Cancer

Capmatinib, the active ingredient of Tabrecta®, is a kinase inhibitor that targets mesenchymal-epithelial transition (MET), including the mutant variant produced by exon 14 skipping. MET exon 14 skipping results in a protein with a missing regulatory domain that reduces its negative regulation leading to increased downstream MET signaling. Capmatinib inhibited cancer cell growth driven by a mutant MET variant lacking exon 14 at clinically achievable concentrations and demonstrated anti-tumor activity in animal models derived from human lung tumors with either a mutation leading to MET exon 14 skipping or MET amplification. It is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping as detected by an FDA-approved test. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). The efficacy of Tabrecta® was assessed in a multicenter, non-randomized, open-label, multi-cohort study (GEOMETRY mono-1) that included patients who were required to have NSCLC with a mutation that leads to MET exon 14 skipping, epidermal growth factor receptor (EGFR) wild-type and anaplastic lymphoma kinase (ALK) negative status, and at least one measurable lesion as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Those with symptomatic CNS metastases, clinically significant uncontrolled cardiac disease, or who received treatment with any MET or hepatocyte growth factor (HGF) inhibitor were not eligible for the study. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). In a non-randomized, open label

study, the overall response rate of Tabrecta® in treatment-naïve patients was 68% and in previously treated patients was 41%.

Recommendation: Tabrecta® to be non-preferred.

Clinical criteria: All non-preferred: A clinical PA is required to confirm appropriate clinical indication for the individual drug request. Specific to each drug all age, clinical testing requirements, previous step therapies, adjunctive drug therapy requirements, and response without disease progression will be also be evaluated for clinical appropriateness. The standard for the appropriate indication will include the FDA label as well as current NCCN guidelines.

Board Decision: The Board unanimously approved the above recommendation.

Tivicay® PD (dolutegravir); **PDL category**- Antiretrovirals

Dolutegravir, the active ingredient of Tivicay® PD, is a human immunodeficiency virus type 1 (HIV-1) antiretroviral agent. It is an integrase strand transfer inhibitor (INSTI) that inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of DNA integration which is essential for the HIV replication cycle. It is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults (treatment-naïve or -experienced) and in pediatric patients (treatment-naïve or -experienced but integrase strand transfer inhibitor [INSTI]-naïve) aged at least 4 weeks and weighing at least 3kg. Tivicay® tablets and Tivicay® PD tablets for oral suspension are not bioequivalent. The relative bioavailability of Tivicay® PD is about 1.6-fold higher than Tivicay®; thus, the 2 dosage forms are not interchangeable on a milligram-per-milligram basis. If a pediatric patient switches from one formulation to the other, the dose must be adjusted for the new dosage formulation. Tivicay® tablets have been available for numerous years and have been found to be safe and effective. Tivicay® tablets have been available for numerous years and have been found to be effective treatment. However, Tivicay® and Tivicay® PD are not bioequivalent and are not interchangeable on a milligram per milligram basis.

Recommendation: Tivicay® PD to be preferred.

Board Decision: The Board unanimously approved the above recommendation.

Trodelvy® (sacituzumab govitecan); **PDL category**- Cancer

Sacituzumab govitecan, the active ingredient of Trodelvy®, is a Trop-2-directed antibody and topoisomerase inhibitor conjugate, composed of the following 3 components

- The humanized monoclonal antibody, hRS7 IgG1κ (also called sacituzumab), which binds to Trop-2 (the trophoblast cell-surface antigen-2)
- The drug SN-38, a topoisomerase inhibitor
- A hydrolysable linker (called CL2A), which links the humanized monoclonal antibody to SN-38.

The recombinant monoclonal antibody is produced by mammalian cells, while the small molecule components SN-38 and CL2A are produced by chemical synthesis. It is indicated for the treatment of adult patients with metastatic triple-negative breast cancer (mTNBC) who have received at least 2 prior therapies 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 confirmatory trials. The efficacy of Trodelvy® was assessed

in a multicenter, single-arm trial that included metastatic triple-negative breast cancer patients who had received at least 2 prior treatments for metastatic disease (N=108). Patients were treated with Trodelvy® until disease progression or intolerance to the therapy. 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 confirmatory trials. In a single-arm study, Trodelvy® had a 33.3% overall response rate.

Recommendation: Trodelvy® to be non-preferred.

Clinical Criteria:

- All non-preferred: A clinical PA is required to confirm appropriate clinical indication for the individual drug request. Specific to each drug all age, clinical testing requirements, previous step therapies, adjunctive drug therapy requirements, and response without disease progression will be also be evaluated for clinical appropriateness. The standard for the appropriate indication will include the FDA label as well as current NCCN guidelines.

Board Decision: The Board unanimously approved the above recommendation.

Xcopri® (cenobamate); **PDL category**- Anticonvulsants

Cenobamate, the active ingredient of Xcopri®, has been shown to reduce repetitive neuronal firing by inhibiting voltage-gated sodium currents. It is also a positive allosteric modulator of the γ-aminobutyric acid (GABA-A) ion channel. However, the exact mechanism by which it exerts its therapeutic effects for its approved indication is not known. It is indicated for the treatment of partial-onset seizures in adult patients. The safety and efficacy of use of Xcopri® were assessed for the treatment of partial-onset seizures in two multicenter, randomized, double-blind, placebo-controlled studies that included adults with partial-onset seizures with or without secondary generalization and who were not adequately controlled with 1 to 3 concomitant antiepileptic drugs (AEDs). In two clinical trials compared with placebo, Xcopri® was found to be significantly more effective than placebo for the percent change from baseline in seizure frequency per 28 days in the treatment period. Comparator studies with other active treatments were not found. There is no evidence at this time to support that Xcopri® is safer or more effective than the currently preferred, more cost-effective medications.

Recommendation: Xcopri® to be non-preferred.

Clinical Criteria:

- Xcopri criteria: History of trials with at least 4 AEDs (2 generic, 2 branded or Uncontrolled seizures on three AEDs; or Uncontrolled on 2 AEDs given along with VNS. Uncontrolled defined as 3 or more TC seizures per year (increases risk of SUDEP); > 6 disabling seizures per year. Any patient who has gone to the ED 2 or more times in the prior 12 months (who has also tried and failed at least 3 other drugs). Ongoing use requires 50 percent reduction in seizure frequency after three months.

Board Decision: The Board unanimously approved the above recommendation.

Zeposia® (ozanimod); **PDL category**- Multiple Sclerosis: Non-Interferons

Ozanimod, the active ingredient of Zeposia®, is a sphingosine 1-phosphate (S1P) receptor modulator that binds with high affinity to S1P receptors 1 and 5. It blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which it exerts its therapeutic effects in multiple sclerosis is not known but may involve the reduction of lymphocyte migration into the CNS. It is indicated for the treatment of relapsing forms of multiple sclerosis (MS) to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Initiate Zeposia® with a 7-day titration, to include 0.23mg PO QD on days 1-4 and then 0.46mg PO QD on days 5-7. After initial titration, the recommended maintenance dosage is 0.92mg PO QD starting on day 8 and thereafter. Swallow capsules whole and administer with or without food. If a dose is missed during the first 2 weeks of treatment, reinitiate treatment using the titration regimen. If a dose is missed after the first 2 weeks of treatment, continue with the treatment as planned. The safety and efficacy of Zeposia® were assessed in 2 randomized, double-blind, double-dummy, parallel-group, active comparator-controlled trials of similar design that included patients with relapsing forms of MS. In clinical trials, adults treated with Zeposia® had a statistically significantly lower ARR over 12 months in one study and over 24 months in a second study as compared with interferon beta-1a 30mcg IM in a population with relapsing MS. While MRI endpoints were also significantly improved with Zeposia® in both studies compared with interferon beta-1a, the pooled analysis of the proportion with 3 month confirmed disability progression was not significantly different between treatments. However, there is no evidence to support that Zeposia® is more effective than interferon beta-1a for confirmed disability progression in the available studies. Since this is the only comparative data found, there is also no evidence found that Zeposia® is safer or more effective than other preferred treatments. It is therefore recommended that Zeposia® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

Recommendation: Zeposia® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Zepzelca® (lurbinectedin); **PDL category**- Cancer

Lurbinectedin, the active ingredient of Zepzelca®, is an alkylating drug that binds guanine residues in the minor groove of DNA, forming adducts and resulting in a bending of the DNA helix towards the major groove. Adduct formation triggers a cascade of events that can affect the subsequent activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in perturbation of the cell cycle and eventual cell death. It is indicated for the treatment of adult with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy. This indication is approved under accelerated approval based on overall 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(s). The safety and efficacy of Zepzelca® were assessed in a multicenter, open label, multi-cohort study that assessed Zepzelca® as a single agent in patients with advanced or metastatic solid tumors. In a cohort of patients with SCLC with disease progression on or after platinum-based chemotherapy, there was a 35% overall response rate (0% complete response and 35% partial response) in patients treated with Zepzelca®.

Recommendation: Zepzelca® to be non-preferred.

Clinical criteria: All non-preferred: A clinical PA is required to confirm appropriate clinical indication for the individual drug request. Specific to each drug all age, clinical testing requirements, previous step therapies, adjunctive drug therapy requirements, and response without disease progression will be also be evaluated for clinical appropriateness. The standard for the appropriate indication will include the FDA label as well as current NCCN guidelines.

Board Decision: The Board unanimously approved the above recommendation.

Zilxi® (minocycline topical foam); **PDL category-** Topical- Acne Preparations

Minocycline, the active ingredient of Zilxi®, is a semi-synthetic derivative of tetracycline. The exact mechanism of action for its approved indication is unknown. It is indicated for the treatment of inflammatory lesions of rosacea in adults. The safety and efficacy of Zilxi® were assessed in two multicenter, randomized, double-blind, vehicle-controlled trials of 12 weeks in duration that included subjects 18 years of age or older with inflammatory lesions of rosacea. It is the first topical minocycline foam FDA approved for topical rosacea. Per the full text study by Stein Gold et al2, patients receiving minocycline foam exhibited a significantly greater reduction in the number of inflammatory lesions ($p=0.0031$ study 1, $p<0.0001$ study 2) and significantly higher rates of IGA treatment success ($p=0.0273$ study 1 and $p=0.0077$ study 2). Comparator studies with active ingredients were not found.

Recommendation: Zilxi® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

Clozaril, Fazaclo ODT, Versacloz (clozapine): Drug Safety Communication - FDA Strengthens Warning That Untreated Constipation Can Lead to Serious Bowel Problems
https://www.fda.gov/safety/medical-product-safety-information/clozaril-fazaclo-odt-versacloz-clozapine-drug-safety-communication-fda-strengthens-warning-untreated?utm_campaign=FDA%20MedWatch%3AClozaril%2C%20Fazaclo%20ODT%2C%20Versacloz%20%28clozapine%29-%20Drug%20Safety%20Communication&utm_medium=email&utm_source=Eloqua
FDA Approves Three Drugs for Nonprescription Use Through Rx-to-OTC Switch Process
https://www.fda.gov/news-events/press-announcements/fda-approves-three-drugs-nonprescription-use-through-rx-otc-switch-process?utm_campaign=022420_PR_FDA%20Approves%20Three%20Drugs%20for%20Nonprescription%20Use&utm_medium=email&utm_source=Eloqua
Singulair (montelukast) and All Montelukast Generics: Strengthened Boxed Warning - Due to Restricting Use for Allergic Rhinitis
https://www.fda.gov/safety/medical-product-safety-information/singulair-montelukast-and-all-montelukast-generics-strengthened-boxed-warning-due-restricting-use?utm_campaign=FDA%20MedWatch%20Singulair%20%28montelukast%29%3A%20Strengthened%20Boxed%20Warning&utm_medium=email&utm_source=Eloqua
FDA Approves Label Changes to SGLT2 Inhibitors Regarding Temporary Discontinuation of Medication Before Scheduled Surgery
http://s2027422842.t.en25.com/e/es?s=2027422842&e=312214&elqTrackId=376c7bc788024cd5a73d955f2e3dcbdc&elq=d700e2d071b343878fdae02a4ebbbf19&elqaid=11643&elqat=1

FDA alerts patients and health care professionals of EpiPen (epinephrine) and EpiPen Jr (epinephrine) auto-injector errors related to device malfunctions and user administration

https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-patients-and-health-care-professionals-epipen-auto-injector-errors-related-device?utm_campaign=FDA%20alerts%20patients%20and%20health%20care%20professionals%20of%20EpiPen%20auto-injector%20errors&utm_medium=email&utm_source=Eloqua

FDA Requests Removal of All Ranitidine Products (Zantac) from the Market
https://www.fda.gov/news-events/press-announcements/fda-requests-removal-all-ranitidine-products-zantac-market?utm_campaign=040120_PR_FDA%20Requests%20Removal%20of%20Ranitidine%20Products%20%28Zantac%29%20from%20the%20Market&utm_medium=email&utm_source=Eloqua

FDA Approves Label Changes for Montelukast (Singulair) Regarding the Potential Risk of Serious Mental Health Side Effects
http://s2027422842.t.en25.com/e/es?s=2027422842&e=328327&elqTrackId=376c7bc788024cd5a73d955f2e3dcbdc&elq=bb3dd6d269764f269f7b497fd4704f1b&elqaid=12344&elqat=1

FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems
http://s2027422842.t.en25.com/e/es?s=2027422842&e=326625&elqTrackId=376c7bc788024cd5a73d955f2e3dcbdc&elq=ac707a3bff784a399dcd62181c0aa736&elqaid=12264&elqat=1

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **December 8, 2020** 5:30pm –8:30pm at the Augusta Armory.