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: 03/12/21
RE: Maine DUR Board **Meeting** minutes from March 9, 2021

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		
Jeffrey Barkin, MD, Change Healthcare	X		
Jan Wright, MaineCare Interim Pharmacy Director	X		
Fran Jensen, MaineCare Medical Director	X		

Guests of the Board: Ed Bosshart, PharmD

CALL TO ORDER: 6:30PM

Jan Wright called the meeting to order at 6:30 PM.

PUBLIC COMMENTS

Lisa Wright from Merck: Highlighted the attributes of Verquovo.
Mahesh Tawney: Highlighted the attributes of Oxlumo.

OLD BUSINESS

DUR MINUTES

The December DUR meeting minutes were accepted.

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE

NPI Update: All MaineCare prescribers must be enrolled in MaineCare in order to have no disruption in billing services effective April 1, 2021. A targeted mailing was completed.

RSV Update: The Office of MaineCare Services (OMS), in coordination with their Pharmacy Benefits Manager Change Healthcare, review data from the National Respiratory and Enteric Virus Surveillance

System (NREVSS) to track the epidemic season for Synagis® (palivizumab). Synagis® is indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients. RSV activity typically occurs between November and March, usually beginning in late November or early December, peaking in January or February, and ending by the end of March or April. The normal determination for the end of Synagis® "season" is when the percent positives on antigen tests is ≤ 10% for two weeks, or the percent positives on PCR tests is ≤ 4% for two consecutive weeks. This year, however, according to Maine's data, the epidemic season for RSV as defined did not occur. Therefore, because Synagis® prophylaxis is of unproven value when administered outside of the RSV season as defined by the Centers for Disease and Prevention (CDC) surveillance reports (https://www.cdc.gov/surveillance/nrevss/rsv/state.html#ME), no further shipments will be authorized **after March 5, 2021.**

Billing Information for COVID-19 Vaccines: Effective January 27, 2021, pharmacies may submit claims for reimbursement for COVID-19 vaccines and their administration retroactive to dates of service on or after January 1st, 2021.

Free rides to COVID vaccine appointments

REVISED CLINICAL CRITERIA/PREFERRED REVIEW

Biosimilars

- Nyvepria (pegfilgrastim- apgf injection) - Biosimilar to Neulasta
- Riabni (rituximab-arrx) - Biosimilar to Rituxan

Recommendation: Nyvepria and Riabni to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

NEW BUSINESS

INTRO: USE OF HYDROXYCHOLOQUINE AND CLOROQUINE PRE- AND POST COVID

Hydroxychloroquine and chloroquine early on were touted as possible treatments for SARS-CoV-2 infections, due to their anti-inflammatory, antiviral and antithrombotic properties. These drugs interfere with autophagy and lysosomal activity, interact with membrane stability and alter signaling pathways and transcriptional activity, which can result in inhibition of cytokine production and modulation of certain co-stimulatory molecules. Data has shown that in invitro it has the capability of inhibiting viral replication of several types, including influenza, HIV and hepatitis viruses. To date, there is no in vitro data suggesting it suppresses SARS-CoV-2. Additionally, the underlying therapeutic effects and mechanisms of action of the drug remain uncertain. On March 28, 2020, the FDA issued an EUA to allow hydroxychloroquine sulfate and chloroquine sulfate donated to the Strategic National Stockpile to be distributed and used for hospitalized COVID-19 patients. On April 24, 2020, after widespread panic buying and prescribing of the drugs in the outpatient setting, along with some adverse events and deaths, the FDA cautioned against their use outside of hospital settings or clinical trials. In the past few months, trials in both the inpatient and outpatient settings have shown no proven benefits from the use of hydroxycholorquine or chloroquine in the treatment of COVID-19 infections and therefore, current recommendations do not support its use for treatment in the inpatient or outpatient settings. Inpatient

trial of 479 patients did not show a benefit in either 14-day clinical status or 28-day mortality, resulting in early termination of the trial. Other open-label trials also showed no benefit early on and the chloroquine arms were terminated early. Outpatient trials have shown no benefit in reducing hospitalization rates or time to symptom resolution. On June 15th, 2020, the FDA revoked the EUA to use hydroxychloroquine and chloroquine to treat COVID in hospitalized patients. We will use paid, non-reversed Medicaid pharmacy and medical claims date from March 2020 – December 2020 excluding members with Part D, MaineRX and TPL. We will look at all members who were prescribed first dose of hydroxychloroquine or chloroquine in either inpatient or outpatient setting, excluding those with a rheumatologic diagnosis of SLE or arthritis. Will look at the number of days prescribed and see if in the outpatient setting, refills were given. We will look for the diagnosis of COVID and see if the number of prescriptions significantly decreased after the June FDA revocation of the EUA, both in medical and pharmacy claims.

Board Decision: None at this time.

PRESENTATION: INFLUENZA VACCINATION RATES

Influenza vaccination rates are routinely significantly lower than recommended by the CDC. Influenza is responsible for many thousands of deaths annually, including among children and those with chronic illnesses. It is somewhat surprising that more people are not immunized, given the many avenues available for immunization, including pharmacies, work sites, sponsored clinics and PCP/medical specialty offices. While children are often the highest group affected by flu every year, immunization rates are dismal, at around 20% annually. This year especially will be critical given COVID-19 illness, which continues to rage throughout the US. Immunization guidelines are that all people above the age of 6 months receive influenza vaccinations yearly, unless there is a history of severe reactions to previous flu shots. Even those with egg allergies are eligible to get the vaccinations, contrary to popular belief. 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 members who were eligible for vaccination in 2019 and determine the rate of vaccination for the 2019-20 flu season. Additionally, we will look at those who were prescribe Tamiflu in 2018-2019 flu season, to see if previous infection had any effect on improving vaccination rates compared with the general public. We will also look at high risk group, those with COPD, to see if there was a better vaccination rate than that of the general public overall, given higher likelihood of severe infection and death. Of all eligible members, only 20% received a flu shot in 2020. Of those who had prescriptions for Tamiflu (or other Flu treatements in 2109, only 5 % went on to get a flu shot in 2020. Additionally, of members in 2020 with a copd related claim, only 20% of them were vaccinated for the flu in 2020. A diagnosis of COPD did not apparently result in a higher rate of flu vaccinations.

Recommendation: Compliance with guidelines recommending flu shots is poor, with only 20% of eligible patients receiving the vaccine, even those in a high -risk group (COPD). Additionally, having the flu (or symptoms that mimic flu) did not increase compliance with flu vaccination the following year. In fact, the rate of vaccination was lower than in the general population. Continued education to the general public about safety and role of vaccinations is warranted.

Board Decision: The Board unanimously approved the above recommendation.

NEW DRUG REVIEW

Barhemsys® (amisulpride injection); **PDL category-** Antiemetic- Anticholinergic/ Dopaminergic

Amisulpride, the active ingredient of Barhemsys®, is a selective dopamine-2 (D2) and dopamine-3 (D3) receptor antagonist. D2 receptors are located in the chemoreceptor trigger zone (CTZ) and respond to dopamine released from the nerve endings. Activation of CTZ relays stimuli to the vomiting center which is involved in emesis. Amisulpride has no appreciable affinity for any other receptor types apart from low affinities for 5-HT2B and 5-HT7 receptors. It is indicated for adults for prevention of postoperative nausea and vomiting (PONV), either alone or in combination with an antiemetic of a different class and treatment of PONV in patients who have received antiemetic prophylaxis with an agent of a different class or have not received prophylaxis. The efficacy of Barhemsys® for the prevention of PONV was assessed in two randomized, double-blind, placebo-controlled, multicenter trials that included patients undergoing general anesthesia and elective surgery. In 4 clinical trials, Barhemsys® reduced PONV in significantly more patients as compared with placebo. Head-to-head studies with other active ingredients were not found. There is no evidence at this time to support that Barhemsys® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Barhemsys® to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Eysuvis® (loteprednol etabonate); **PDL category-** Op. Of Interest

Loteprednol etabonate, the active ingredient of Eysuvis®, is a corticosteroid. Corticosteroids inhibit the inflammatory response to a variety of inciting agents and delay or slow healing. Corticosteroids inhibit the edema, fibrin deposition, capillary dilation, leukocyte migration, capillary proliferation, fibroblast proliferation, deposition of collagen, and scar formation associated with inflammation. Corticosteroids are thought to inhibit prostaglandin production. It is indicated for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease. The safety and efficacy of Eysuvis® for the treatment of dry eye disease were assessed in 4 multicenter, randomized, double-masked, placebo-controlled trials. The use of artificial tears was not allowed during the trials. Patients with dry eye disease received either Eysuvis® or vehicle four times a day for 2 weeks. In 4 clinical studies, Eysuvis® was more effective than vehicle for reducing ocular discomfort and conjunctival hyperemia. The clinical trials, though demonstrating statistical significance, are of uncertain clinical significance given the relatively small absolute effect of Eysuvis® compared to placebo. There is no evidence at this time to support that Eysuvis® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Eysuvis® to non-preferred.

Clinical Criteria:

- For the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease.

Board Decision: The Board unanimously approved the above recommendation.

Fyavolv® (norethindrone acetate & ethinyl estradiol); **PDL category**- Estrogen Combos

Endogenous estrogens are mainly responsible for the development and the maintenance of the female reproductive system and secondary sexual characteristics. Estrogens act through binding to nuclear receptors in estrogen-responsive tissues. Circulating estrogens modulate the pituitary secretion of the gonadotropins, luteinizing hormone (LH) and follicle stimulating hormone (FSH) through a negative

feedback mechanism. Ethinyl estradiol is an estrogen and the pharmacological effects of ethinyl estradiol are similar to those of endogenous estrogens. It is indicated for the treatment of moderate to severe vasomotor symptoms due to menopause, the prevention of postmenopausal osteoporosis and when prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and non-estrogen medication should be carefully considered. A 12-week placebo-controlled, multicenter, randomized study included symptomatic women (N=266) who had at least 56 moderate to severe hot flushes during the week prior to randomization. On average, patients had 12 hot flushes per day upon study entry. Norethindrone/ethinyl estradiol 1/5 was significantly better than placebo for the relief of the frequency and for relief of the severity of moderate to severe vasomotor symptoms in symptomatic women with moderate to severe hot flushes. In a separate study, postmenopausal women treated with norethindrone aetate/ethinyl estradiol 1/5 had an average increase of 3.1% in lumbar spine BMD, and the difference from placebo (with placebo having an average decrease of -6.3%) was statistically significant. Furthermore, the indication states that when prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and non-estrogen medication should be carefully considered.

Recommendation: Fyavolv® to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Impeklo® (clobetasol propionate lotion) **PDL category-** Topical- Corticosteroids, Very High Potency

Clobetasol propionate, the active ingredient of Impeklo® lotion, is a synthetic fluorinated corticosteroid for topical use. Corticosteroids play a role in cellular signaling, immune function, inflammation, and protein regulation; however, the exact mechanism of action in corticosteroid-responsive dermatoses is not known. Impeklo® lotion is in the super-high range of potency as demonstrated in vasoconstrictor studies in healthy subjects when compared with other topical corticosteroids. However, similar blanching scores do not necessarily imply therapeutic equivalence. It is indicated for relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses in patients 18 years of age or older. Limitations of use include that it should not be used in the treatment of rosacea or perioral dermatitis. In addition, use in patients under 18 years of age is not recommended due to numerically high rates of HPA axis suppression. The efficacy of clobetasol propionate 0.05% lotion was assessed and demonstrated in two trials that included subjects with either moderate to severe plaque psoriasis or moderate to severe atopic dermatitis. Clobetasol lotion was superior to placebo in both trials. The studies included in the Impeklo® lotion 0.05% clinical trials section were the same as those in the clinical trials section of Clobex®, also a clobetasol propionate 0.05% lotion. Brand Clobex® is not currently rebatable under the Medicaid program, but a generic for Clobex® lotion is still available. The generic for Clobex® has been available for many years and is a safe and effective product.

Recommendation: Impeklo® lotion be non-preferred.

Clinical Criteria:

- For the treatment of patients ≥ 18 years of age.

Board Decision: The Board unanimously approved the above recommendation.

Monjuvi® (tafasitamab-cxix); **PDL category**- Cancer

Tafasitamab-cxix, the active ingredient of Monjuvi®, is a humanized CD19-directed cytolytic monoclonal antibody that contains an IgG1/2 hybrid Fc-domain with 2 amino acid substitutions to modify the Fc-mediated functions of the antibody. It binds to CD19 antigen expressed on the surface of pre-B and mature B lymphocytes and on several B-cell malignancies, including diffuse large B-cell lymphoma (DLBCL). Upon binding to CD19, tafasitamab-cxix mediates B-cell lysis through apoptosis and immune effector mechanisms, including antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). In studies conducted in vitro in DLBCL tumor cells, tafasitamab-cxix in combination with lenalidomide resulted in increased ADCC activity compared to tafasitamab-cxix or lenalidomide alone. It is indicated in combination with lenalidomide, for the treatment of adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant (ASCT). This indication is approved under accelerated approval based on overall response rate. 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 Monjuvi® in combination with lenalidomide followed by Monjuvi® as monotherapy were assessed in an open-label, multicenter, single-arm study that included patients with relapsed or refractory DLBCL after 1 to 3 prior systemic therapies, including a CD20-directed cytolytic antibody and who were not candidates for high dose chemotherapy followed by autologous stem cell transplantation (ASCT). In a single-arm, open-label study, the best overall response rate with Monjuvi® was 55%.

Recommendation: Monjuvi® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Orladeyo® (berotralstat); **PDL category**- Hereditary Angioedema- Prophylaxis

Berotralstat, the active ingredient of Orladeyo®, is a plasma kallikrein inhibitor that binds to plasma kallikrein and inhibits its proteolytic activity. Plasma kallikrein is a protease that cleaves high molecular weight kininogen (HMWK) to generate cleaved HMWK (cHMWK) and bradykinin, a potent vasodilator that increases vascular permeability resulting in swelling and pain associated with hereditary angioedema (HAE). In patients with HAE due to C1-inhibitor (C1-INH) deficiency or dysfunction, normal regulation of plasma kallikrein activity is not present, which leads to uncontrolled increases in plasma kallikrein activity and results in angioedema attacks. Berotralstat decreases plasma kallikrein activity to control excess bradykinin generation in patients with HAE. It is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years of age and older. The safety and efficacy of Orladeyo® for the treatment of acute HAE attacks have not been established. Orladeyo® should not be used for treatment of acute HAE attacks. Additional doses or doses of Orladeyo® higher than 150mg once daily are not recommended due to the potential for QT prolongation. The efficacy of Orladeyo® for the prevention of angioedema attacks in patients 12 years of age and older with Type 1 or II HAE was assessed in Part 1 of a multicenter, randomized, double-blind, placebo-controlled, parallel-group study.

Recommendation: Orladeyo® be non-preferred.

Clinical Criteria:

- Clinical PA is required to establish diagnosis and medical necessity.
- For the treatment of patients ≥ 12 years of age.

Board Decision: The Board unanimously approved the above recommendation.

Oxlumo® (lumasiran); **PDL category**- Primary Hyperoxaluria Type 1 (PH1)

Lumasiran, the active ingredient of Oxlumo®, is an HAO1-directed double-stranded small interfering ribonucleic acid (siRNA), covalently linked to a ligand containing N-acetyl galactosamine (GalNAc). Lumasiran reduces levels of glycolate oxidase (GO) enzyme by targeting the hydroxy acid oxidase 1 (HAO1) messenger ribonucleic acid (mRNA) in hepatocytes through RNA interference. Decreased GO enzyme levels reduce the amount of available glyoxylate, a substrate for oxalate production. As the GO enzyme is upstream of the deficient alanine-glyoxylate aminotransferase (AGT) enzyme that causes PH1, the mechanism of action of lumasiran is independent of the underlying AGXT gene mutation. Oxlumo® is not expected to be effective in primary hyperoxaluria type 2 (PH2) or type 3 (PH3) because its mechanism of action does not affect the metabolic pathways causing hyperoxaluria in PH2 and PH3. It is indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients. The safety and efficacy of Oxlumo® were assessed in a randomized, double-blind study comparing lumasiran and placebo in patients 6 years of age and older with PH1 and an eGFR ≥30ml/min/1.73m2. In a small study that included 39 patients with ages ranging from 6 to 61 years, the least square mean % change from baseline in 24-hour urinary oxalate was -65% with Oxlumo® as compared with -12% with placebo, which was statistically significantly different.

Recommendation: Oxlumo® be non-preferred.

Clinical Criteria:

- New category PRIMARY HYPEROXALURIA TYPE 1 (PH1)
- PA is required to establish diagnosis and medical necessity.

Board Decision: The Board unanimously approved the above recommendation.

Phexxi® (lactic acid, citric acid, potassium bitartrate); **PDL category**- Contraceptives: Patches/Vaginal Products

In vitro studies demonstrated that a pH lowering effect and sperm motility reduction contributed to the activity of Phexxi® in the vagina. Pharmacokinetic studies have not been performed. It is indicated for the prevention of pregnancy in females of reproductive potential for use as an on-demand method of contraception. Phexxi® is not effective for the prevention of pregnancy when administered after intercourse. The efficacy of Phexxi® for the prevention of pregnancy was assessed in a multicenter, open-label, single-arm study in the United States. The study enrolled females of reproductive potential aged 18 to 35 years with regular menstrual cycles (21 to 35 days), with the median age of the included females being 27.8 years. Phexxi® is a first in its class, being a non-hormonal agent available via prescription that works immediately for the prevention of pregnancy. It is not effective for the prevention of pregnancy when administered after vaginal intercourse. Phexxi® should be avoided with a vaginal ring. In an open-label, single-arm study, the 7-cycle cumulative pregnancy rate of Phexxi® was 13.7% and the estimated Pearl Index, calculated based on data from the 7-cycle study, was 27.5. To provide some basis for comparison, another contraceptive method, the Annovera® vaginal ring that contains segesterone acetate and ethinyl estradiol, has an overall pooled unintended pregnancy rate (Pearl Index) of 2.98 per 100 woman-years2 and condoms are generally cited as having a Pearl Index of 3-123. There is no evidence at this time to support that Phexxi® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Phexxi® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

RediTrex® (methotrexate injections); **PDL category**- Rheumatoid Arthritis

Methotrexate, the active ingredient of RediTrex®, is a folate analog metabolic inhibitor that inhibits dihydrofolic acid reductase. Dihydrofolates must be reduced to tetrahydrofolates by this enzyme before they can be utilized as carriers of one-carbon groups in the synthesis of purine nucleotides and thymidylate. Thus, methotrexate interferes with DNA synthesis, repair, and cellular replication. Actively proliferating tissues such as malignant cells, bone marrow, fetal cells, buccal and intestinal mucosa, and cells of the urinary bladder are in general more sensitive to this effect of methotrexate. It is indicated for Rheumatoid arthritis (RA) including polyarticular juvenile idiopathic arthritis, in the management of selected adults with severe, active RA (ACR criteria), or children with active polyarticular juvenile idiopathic arthritis (pJIA), who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs). And Psoriasis: in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis 'flare' is not due to an undiagnosed concomitant disease affecting immune responses. Clinical trials in patients with rheumatoid arthritis and polyarticular juvenile idiopathic arthritis were performed using other formations of methotrexate. Most studies of methotrexate in patients with RA were relatively short. Methotrexate has been available for numerous decades and has been found to be a relatively safe and effective product. Numerous dosage forms, including oral and injectable and as brand and generics are available. RediTrex® is a new methotrexate delivery system of pre-filled syringes intended for ease of handling and dosing in patients with RA/pJIA and psoriasis. It is important to ensure that a psoriasis 'flare' is not due to an undiagnosed concomitant disease affecting immune responses. RediTrex® is not indicated for the treatment of neoplastic diseases. Methotrexate is an effective treatment that has been available for numerous years in various dosage forms. RediTrex® is a new delivery system for methotrexate, in prefilled syringes for subcutaneous administration, offering patients a new option.

Recommendation: Reditrex® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Sutab® (sodium sulfate, magnesium sulfate, and potassium chloride); **PDL category**- GI, Miscellaneous

The primary mode of action of Sutab® is osmotic action of sodium sulfate and magnesium sulfate, which induce a laxative effect. The physiological consequence is increased water retention in the lumen of the colon, resulting in loose stools. It is indicated for the cleansing of the colon as a preparation for colonoscopy in adults. The safety and efficacy of Sutab® for colon cleansing were assessed in 2 randomized, single-blind, active-controlled multicenter studies that included adult subjects undergoing colonoscopy for colorectal cancer screening and surveillance, or diagnostic colonoscopy, including subjects with abdominal pain, diarrhea, constipation, and non-severe inflammatory bowel disease. The primary efficacy endpoint in each study was the proportion of patients with successful colon cleansing, as assessed by the blinded person performing the colonoscopy utilizing the 4-point scale described below. Success was defined as an overall cleansing assessment of 3 (good) or 4 (excellent). two studies to assess the efficacy of Sutab® with active comparators that included adults undergoing colonoscopy for colorectal

cancer screening and surveillance, or diagnostic colonoscopy, Sutab® was non-inferior to the active comparator for the primary endpoint of the proportion of patients with successful colon cleansing.

Recommendation: Sutab® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Twirla® (levonorgestrel and ethinyl estradiol); **PDL category**- Contraceptives- Patches/Vaginal Products

Combined hormonal contraceptives (CHCs) lower the risk of becoming pregnant primarily by suppressing ovulation. Twirla® is a combination of levonorgestrel (a progestin) and ethinyl estradiol (an estrogen). It is indicated as a method of contraception for use in women of reproductive potential with a BMI <30 kg/m2 for whom a combined hormonal contraceptive is appropriate. The efficacy of Twirla® was assessed in one open-label, single arm, multicenter study in the U.S. that included women ranging in age between 18 to 60 years (N=2,031) who were healthy and sexually active with regular menstrual cycles. Consider the reduced effectiveness of Twirla® in women with a BMI ≥25 to <30kg/m2 before prescribing Twirla®. Twirla® is contraindicated in women with a BMI ≥30kg/m2. In an open-label, single-arm study that included healthy and sexually active women aged 18 to 35 years, the overall Pearl Index was 5.8; however, there were clear differences in efficacy by BMI category. The Pearl Index for women with a BMI <25kg/m2 was 3.5. There was an increase in pregnancy rate as BMI increased based on the primary analysis population (N=1,735). There is no evidence at this time to support that Twirla® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Twirla® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Verquvo® (vericiguat); **PDL category**- Cardiac- Soluble Guanylate Cyclase Stimulators

Vericiguat, the active ingredient of Verquvo®, is a soluble guanylate cyclase stimulator. Soluble guanylate cyclase (sGC) is an important enzyme in the nitric oxide (NO) signaling pathway. When NO binds to sGC, the enzyme catalyzes the synthesis of intracellular cyclic guanosine monophosphate (cGMP), a second messenger that plays a role in the regulation of vascular tone, cardiac contractility, and cardiac remodeling. Heart failure is associated with impaired synthesis of NO and decreased activity of sGC, which may contribute to myocardial and vascular dysfunction. By directly stimulating sGC, independently of and synergistically with NO, vericiguat augments levels of intracellular cGMP, leading to smooth muscle relaxation and vasodilation. It is indicated to reduce the risk of cardiovascular death and heart failure (HF) hospitalization following a hospitalization for heart failure or need for outpatient IV diuretics, in adults with symptomatic chronic HF and ejection fraction less than 45%. The efficacy of Verquvo® was assessed in a randomized, double-blind, placebo-controlled, parallel-group, event-driven, multicenter study (VICTORIA) that included adult patients (N=5,050) with symptomatic chronic heart failure (New York Heart Association [NYHA] class II-IV) and left ventricular ejection fraction (LVEF) less than 45% following a worsening heart failure event. A worsening heart failure event was defined as heart failure hospitalization within 6 months before randomization or use of outpatient IV diuretics for heart failure within 3 months before randomization. In a clinical study assessing the safety and efficacy vericiguat, the primary endpoint of death from cardiovascular causes or hospitalization for heart failure was significantly reduced in the Verquvo® group as compared with placebo. A 2020 systematic review and network meta-analysis (NMA) by Aimo et al2 included 6 randomized controlled trials (4 were phase 3 studies) or subgroup analyses from

randomized controlled trials to assess the effects of sacubitril/valsartan, vericiguat, and SGLT2 inhibitors (dapagliflozin and empagliflozin) with the respective control arms (standard-of-care, SOC) on heart failure with reduced ejection fraction (HFrEF). The primary outcome was cardiovascular death or first HF hospitalization. Annualized event rates for cardiovascular death and/or HF hospitalization were also assessed. Results suggested that all of the available treatments conferred a survival benefit in patients with HFrEF. SGLT2 inhibitors demonstrated the greatest relative reduction in the occurrence of the primary outcome as compared to SOC (HR 0.74). In this analysis, SGLT2i were found to be more effective than sacubitril/valsartan and vericiguat, although statistical significance was not reached for the most clinically relevant outcomes of CV death or HF hospitalization and CV death alone. SGLT2i proved significantly more effective than vericiguat, but not than sacubitril/valsartan for the endpoint "first HF hospitalization." Accordingly, SGLT2i had a higher SUCRA score (a synthetic measure of efficacy) than sacubitril/valsartan, which in turn ranked higher than vericiguat. It is important to stress that these results are preliminary and hypothesis generating, given the indirect nature of the comparison, and dedicated head-to-head comparisons between different therapeutic options should be designed. The authors concluded that based on indirect comparisons, SGLT2 inhibitor therapy is not associated with a significantly lower risk of cardiovascular death or HF hospitalization or cardiovascular death alone compared to sacubitril/valsartan or vericiguat. The risk of HF hospitalization did not differ significantly between patients on SGLT2 inhibitors or sacubitril/valsartan, while dapagliflozin was superior to vericiguat.

Recommendation: Verquvo® be non-preferred.

Clinical Criteria:

- Add new category CARDIAC- SOLUBLE GUANYLATE CYCLASE STIMULATORS

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

New studies show diabetes drug not proven to improve blood sugar control in pediatric patients
https://www.fda.gov/drugs/drug-safety-and-availability/new-studies-show-diabetes-drug-not-proven-improve-blood-sugar-control-pediatric-patients?utm_medium=email&utm_source=govdelivery

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **June 9, 2021** 5:30pm –8:30pm at the Augusta Armory.