Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

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TO: Maine Drug Utilization Review Board
DATE: 3/12/20
RE: Maine DUR Board **Meeting** minutes from March 10, 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		
Jeffrey Barkin, MD, 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

Patricia Jacob from Allergan: Highlighted the attributes of Obrelvy.
Tina Riley a resident: Highlighted the attributes of Vyondys.
Shannon Barrett from Avexis: Highlighted the attributes of Zolgensma.
Kathrine Kocharski from Sarepta: Highlighted the attributes of Vyondys.
Lauren Lennon from GBT: Highlighted the attributes of Oxbryta.

OLD BUSINESS

DUR MINUTES

The December DUR meeting minutes were accepted.

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE

No update at this time.

REVISED CLINICAL CRITERIA/PREFERRED REVIEW

Biosimilars:

Kanjinti® **PDL category-** Antineoplastics- Monoclonal Antibodies

Ogivri® **PDL category-** Antineoplastics- Monoclonal Antibodies

Ruxience® **PDL category-** Cancer

Truxima® **PDL category-** Cancer

Ziextenzo® **PDL category-** Granulocyte CSF

Zirabev® **PDL category-** Cancer

Recommendation: Add all to non-preferred

Board Decision: The Board unanimously approved the above recommendation.

NEW BUSINESS

DATA PRESENTATION: USE OF STATINS IN MEMBERS WITH DIABETES MELLITUS

Guidelines for the treatment of diabetes mellitus due to the vascular effects of elevated blood sugar include lifestyle changes, including diet and exercise, management of hypertension and lipid-lowering therapy. Both micro and macrovascular complications are high in the diabetic population and increase as diabetics age. Among the most common complications are myocardial infarctions, peripheral vascular disease and strokes. ASCVD is the leading cause of morbidity and mortality in DM, and annual spending related to CV complications of DM recently topped 37 billion dollars. Over the past decade however the 10-year CHD risk has improved and ASCVD morbidity and mortality have decreased, likely in large measure due to efforts to lower cholesterol levels. Multiple trials have shown the benefits of lowering cholesterol in those with and without ASCVD. 14 randomized clinical trials including 18,000 patients have shown a 9% reduction in all-cause mortality and 13% reduction in vascular mortality for every 39mg/dl decrease in LDL. Current recommendations are that in patients over the age of 40, or in those with CVD, statins should be added to the treatment regimen, which includes lifestyle changes, regardless of baseline lipid levels. Additionally, lipid therapy should be considered in those under 40 who have multiple cardiac risk factors. Which statin to use, and the target dose, is based on the patient's CVD risk, side effects, tolerability and LDL cholesterol level. Those who have known CVD should aim for high-intensity statin therapy. 2019 ADA guidelines recommend high intensity statin therapy in those under 40 who have ASCVD and those whose 10-year risk exceeds 20%. In those over 40 without ASCVD risk of greater that 20%, moderate intensity statin therapy is recommended, while high intensity therapy is recommended in all others. In both age groups, if LDL remains above 70 in the high- risk patients, consideration should be given to adding a PCSK9 therapy or ezetimibe. Even in those unable to tolerate

moderate or high intensity therapy, low doses of statins have been shown to confer benefit. Identified members with a diagnosis of DM, either type 1 or 2, stratify by age, and cardiovascular disease and look to see whether there has been at least one prescription for a statin within the year. Of those prescribed statin therapy, evaluate compliance with therapy during the year and the level of statin therapy prescribed (high, moderate or low intensity statin). For those who did not have a prescription for the initial statin for the entirety of the year, see who was prescribed a different statin, presumably due to intolerance of the initial statin prescribed, and whether this statin was continued for the rest of the year. For members with both Diabetes and CVD, there were 2191 prescriptions for statins. Of those, only 81 were for low-intensity statins, the rest were either intermediate or high-intensity. This shows good compliance with guidelines. Some of those 81 prescriptions were written for members who had a previous prescription for a higher intensity statin and likely had issues with side effects that required dropping the dosage.

Recommendation: Most members who have cardiovascular disease are on appropriate statin therapy and the high percentage of those who were prescribed multiple GPIs suggest that providers attempted to find the best tolerated and perhaps highest intensity statin that could be tolerated. IN the diabetics without CVD, there was less compliance with ADA and AHA guidelines that indicate statins should be used more widely in diabetics above the age of 40. We recommend that a review of the guidelines highlighting the recommendations be published in the Medicaid bulletin sent to providers and that the data be collected again a year after the bulletin is published, to evaluate whether practice behavior has changed.

Board Decision: The Board unanimously approved the above recommendation.

DATA PRESENTATION: USE OF BUPRENORPHINE FOR MAT

Opioid use disorder is now a major public health problem. While the recognition of the problem has curbed the use of opioids for management of acute and chronic pain, there are a tremendous number of people who are addicted. They need medication assisted therapy to both discontinue use of opioids and to maintain abstinence. While there are several drugs that can be used by far the safest and overall most effective and widely used is buprenorphine, either alone or in combination with naltrexone. All medications used for MAT, however, have the potential for abuse. The goal is to find the lowest possible dose that will induce a remission and maintain abstinence. While it once was thought that a limited time of treatment was advisable, we now know that many patients will need indefinite use. The maximum recommended dose for initiation is 32mg daily, and while it generally is advisable to have no higher than 16mg daily for maintenance, many patients will be able to avoid having cravings at much lower doses. We will use paid, non-reversed Medicaid pharmacy and medical claims date from calendar year 2019 excluding members with Part D, MaineRX and TPL. Identified those members on buprenorphine any time in 2019, without any lapse in treatment. We will identify the initiation dose for the member for the first 60 days of treatment. We will average the dose for day 61 forward and separately look at the average dose for the last 60 days of treatment. Many members have been on buprenorphine for years, so the full analysis will encompass those started on buprenorphine from 11/18 on to capture those who have been on buprenorphine for the full year 2019. Will evaluate the number of members on higher than 16mg daily for maintenance and since this requires prior approval, evaluate the reasons for the higher dose.

Recommendation: Given the lack of data supporting the need for more than 16mg/day as maintenance therapy, do chart reviews on the 56 members getting more than 16mg/day. Identify reasons for higher dose (including induction) and see if there are a small number of providers prescribing higher dose for maintenance, or if it is a more widespread problem. A targeted education for providers overprescribing may be warranted, depending on the findings.

Board Decision: No action needed at this time.

INTRODUCE: PRESCRIBER PDL COMPLIANCE (PICK 6 CATEGORIES)

Pharmacy formularies are constructed to guide providers in the commercial insurer world to use efficacious and cost-effective therapies in accordance with covered products. For Medicaid, the Preferred Drug List (PDL) is constructed with all out-patient drugs being available in accordance with Social Security Act 1927 and is posted publicly. While not mandated by Social Security Act 1927, states are allowed to maintain a Preferred Drug List and to enter rebate agreements with manufacturers to maximize savings while guaranteeing access and quality. The criteria used to determine authorization for non-preferred drugs is transparent and vetted through the state Pharmacy and Therapeutics Committee. These criteria for prescribing non-preferred medications are posted on the PDL. While not meant to be burdensome for providers, a well- constructed PDL should allow for prescribing of appropriate medications in most circumstances without requiring prior authorization of non-preferred medications. Evaluating the compliance with prescribing of preferred medications is a way to evaluate the rigor and adherence to criteria of the PA process. Additionally, if the PA process is sound, and many members are getting non-preferred medications appropriately, it may indicate a need to reevaluate the medication class and possible reorganization of preferred and non-preferred drug categorizations. States strive to stay current with new drugs and new indications for established medications, making PDLs fluid documents that change regularly. Auditing compliance of major drug classes is a way to monitor performance of pharmacy benefit management.

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 evaluate these following categories to see how often the dispensed medication was preferred for the following categories:

- Multiple sclerosis: interferon and non-interferon medications
- Diabetes mellitus: incretin mimetics (GLP1 agonists and DPP-4 inhibitors)
- Hypercholesterolemia: statins and more potent drugs and combinations (ezetimibe, Repatha, Praluent)
- Seizure disorders: anticonvulsants
- Asthma: inhaled corticosteroids, beta adrenergic agonists and combination inhalers

We will audit a sampling of charts in each category to evaluate the adherence to criteria for approval of non-preferred medications.

Board Decision: No action

NEW DRUG REVIEW

Absorica® (isotretionoin capsule); **PDL category-** Topical- Oral

Isotretinoin, the active ingredient of Absorica® LD, is a retinoid. When administered at the recommended dosage, it inhibits sebaceous gland function and keratinization. Clinical improvement in nodular acne patients occurs in association with a reduction in sebum secretion. The decrease in sebum secretion is temporary and is related to the dose and duration of treatment with isotretinoin capsules and reflects a reduction in sebaceous gland size and an inhibition of sebaceous gland differentiation. The exact mechanism of action for the treatment of its approved indication is unknown. It is indicated for the treatment of severe recalcitrant nodular acne in non-pregnant patients 12 years of age and older with multiple inflammatory nodules with a diameter of 5mm or greater. Because of significant adverse reactions associated with its use, Absorica® LD is reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics. If a second course of Absorica® LD therapy is needed, it is not recommended before a two-month waiting period because the patient's acne may continue to improve following a 15 to 20-week course of therapy. The safety and efficacy of Absorica/Absorica® LD for the treatment of severe recalcitrant nodular acne has been established and is based on a double-blind, randomized, parallel group study that included patients 12 years of age and older who received Absorica® or another isotretinoin capsule product. Given that the bioavailability and the recommended dosage of Absorica® and Absorica® LD are different, the two are not substitutable. Absorica® has been available for numerous years, as well as a generic isotretinoin.

Recommendation: Absorica® LD to non-preferred.

Clinical Criteria:

- Rename category to isotretinoin, Acne
- Add Myorisan and Zenatane to preferred
- Add Absorica to non-preferred
- 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.

Adakveo® (crizanlizumab-tmca); **PDL category-** Sickle Cell Disease

Crizanlizumab-tmca is a selectin blocker humanized IgG2 kappa monoclonal antibody that binds to P-selectin and blocks interactions with its ligands, including P-selectin glycoprotein ligand 1. Binding P-selectin on the surface of the activated endothelium and platelets block interactions between endothelial cells, platelets, red blood cells, and leukocytes. It is indicated to reduce the frequency of vaso-occlusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease. The safety and efficacy of Adakveo® were assessed in patients with sickle cell disease (SCD) in a randomized, multicenter, placebo-controlled, double-blind study of 52 weeks in duration. In the SUSTAIN study, it was found to significantly lowered the median annual rate of VOC compared to placebo. In addition, more in the Adakveo® group did not experience a VOC (NNT 6), while the median time to the first VOC was 4.1 months with Adakveo® vs 1.4 months with placebo.

Recommendation: Adakveo® to non-preferred.

Clinical Criteria:

- Adakveo is indicated to reduce the frequency of vaso-occlusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease.

Board Decision: The Board unanimously approved the above recommendation.

Amzeeq® (minocycline aerosol); **PDL category**- Topical-Acne Preparations

Minocycline, the active ingredient of Amzeeq®, is a semi-synthetic derivative of tetracycline. Its mechanism of action for the treatment of acne is not known. It is indicated for the topical treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in adults and pediatric patients 9 years of age and older. This formulation of minocycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, Amzeeq® should be used only as indicated. The safety and efficacy of Amzeeq® were assessed in three multicenter, randomized, double-blind, vehicle-controlled studies of 12 weeks in duration that included subjects with moderate to severe acne vulgaris. Amzeeq® is the first topical minocycline available on the market, and it was found to be effective in clinical trials as compared with vehicle for treatment success and inflammatory lesion count change. The propellant in Amzeeq® is flammable and thus the patient should avoid fire, flame, and smoking during and immediately after application.

Recommendation: Amzeeq® Lotion to non-preferred.

Clinical Criteria:

- For the treatment of patients ≥ 9 years of age.

Board Decision: The Board unanimously approved the above recommendation.

Asceniv® (immune globulin IV, human-slra); **PDL category**- Immune Globulins

Asceniv® is a replacement therapy for patients which contains mainly immunoglobulin G (IgG) with a broad spectrum of antibodies against various infectious agents. It is prepared from pooled plasma from not less than 1000 donors, has an IgG subclass distribution similar to that of native human plasma. Adequate doses of IGIV can restore an abnormally low IgG level to the normal range. The manufacturing process includes 3 steps to remove/inactivate adventitious viruses to minimize the risk of virus transmission. The broad spectrum of neutralizing IgG antibodies against bacterial and viral pathogens and their toxins help to avoid recurrent serious opportunistic infections. IgG antibodies are opsonins that increase phagocytosis and elimination of pathogens from the circulation. However, the mechanism of action for its indication has not been fully explained. It is indicated as a 10% immune globulin liquid for IV injection indicated for the treatment of primary humoral immunodeficiency (PI) in adults and adolescents (12 to 17 years of age). PI includes but is not limited to the humoral immune defect in congenital agammaglobulinemia, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies (SCID). Asceniv® has a box warning regarding thrombosis, renal dysfunction, and acute renal failure. A prospective, open-label, single-arm multicenter study assessed the safety and efficacy of Asceniv® in patients with primary humoral immunodeficiency. PI includes, but is not limited to, the humoral immune defect in congenital agammaglobulinemia, common variable immunodeficiency (CVID), X-linked agammaglobulinemia,

Wiskott-Aldrich syndrome, and severe combined immunodeficiencies. In an open-label, single-arm 12-month study, there were no serious acute bacterial infections that occurred in patients treated with Asceniv®.

Recommendation: Asceniv® Sprinkles be non-preferred.

Clinical Criteria:

- For the treatment of patients between 12 to 17 years of age.
- Asceniv indicated for the treatment of primary humoral immunodeficiency (PI) in adults and adolescents (12 to 17 years of age). PI includes but is not limited to the humoral immune defect in congenital agammaglobulinemia, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies (SCID).

Board Decision: The Board unanimously approved the above recommendation.

Beovu® (brolucizumab-dbll); **PDL category**- OP- Of Interest

Brolucizumab-dbll, the active ingredient of Beovu®, is a recombinant human vascular endothelial growth factor (VEGF) inhibitor. Brolucizumab binds to the 3 major isoforms of VEGF-A, thus preventing interaction with receptors VEGFR-1 and VEGFR-2. By inhibiting VEGF-A, brolucizumab suppresses endothelial cell proliferation, neo-vascularization, and vascular permeability. It is indicated for the treatment of Neovascular (wet) Age-Related Macular Degeneration (AMD). The safety and efficacy of Beovu® were assessed in 2 randomized, multicenter, double-masked, active-controlled studies that included patients with wet AMD (N=1817) treated for 2 years. In 2 clinical trials compared with active comparator aflibercept, Beovu® had a similar mean change from baseline in best-corrected visual acuity. In addition, through week 48, over 50% in each study remained on Beovu® every 12-week dosing and aflibercept dosed every 8 weeks.

Recommendation: Beovur® to be non-preferred.

Clinical Criteria:

- Beovu is non-preferred and indicated for the treatment of Neovascular (wet) Age-Related Macular Degeneration (AMD).
- Add Lucentis to non-preferred on the PDL.

Board Decision: The Board unanimously approved the above recommendation.

Brukinsa® (zanubrutinib); **PDL category**- Cancer

Zanubrutinib, the active ingredient of Brukinsa®, is a Bruton's tyrosine kinase (BTK) inhibitor. It is a small-molecule inhibitor of BTK that forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK activity. BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. In non-clinical studies, zanubrutinib inhibited malignant B-cell proliferation and reduced tumor growth. It is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. 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. The safety and efficacy of Brukinsa® were assessed in a Phase 2, open-label, multicenter, single-arm trial (Study 1) that included previously treated patients with MCL (N=86) who had received at least one prior therapy. 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. The efficacy of Brukinsa® was seen in two open-label, single-arm studies, with overall response rate being 84% in both studies.

Recommendation: Brukinsa® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Clovique® (Trientine); **PDL category**- Chelating Agents

Trientine, the active ingredient of Clovique®, is a chelating compound for removal of excess copper from the body. Wilson's disease is an autosomal inherited metabolic defect resulting in an inability to maintain a near-zero balance of copper. Excess copper accumulates, perhaps because the liver lacks the mechanism to excrete free copper into the bile. This condition is treated with a low copper diet and the use of chelating agents that bind copper to facilitate its excretion from the body. It is indicated in the treatment of patients with Wilson's disease who are intolerant of penicillamine. Clinical experience with trientine HCl is limited and alternate dosing regimens have not been well-characterized; all endpoints in determining an individual patient's dose have not been well defined. Clovique® and penicillamine cannot be considered interchangeable, and Clovique® should be used when continued treatment with penicillamine is no longer possible because of intolerable or life endangering side effects. Unlike penicillamine, Clovique® is not recommended in cystinuria or rheumatoid arthritis. It is not indicated for treatment of biliary cirrhosis. The data available in the clinical trials for Clovique® were those seen with Syprine®, which has the same active ingredient as Clovique® but has been available for numerous years. Syprine® also has a generic. Clovique® was formulated to have room temperature stability for up to 30 days, being in a portable blister pack.

Recommendation: Clovique® Pen be non-preferred.

Clinical Criteria:

- Clovique® should be used when continued treatment with penicillamine is no longer possible because of intolerable or life endangering side effects
- Add Syprine and Trientine Caps to non-preferred on the PDL.

Board Decision: The Board unanimously approved the above recommendation.

Enhertu® (fam-trastuzumab deruxtecan-nxki); **PDL category**- Antineoplastices- Monoclonal Antibodies

Fam-trastuzumab deruxtecan-nxki, the active ingredient of Enhertu®, is a HER2-directed antibody and topoisomerase inhibitor conjugate. It is an antibody-drug conjugate composed of 3 components, including 1.) a humanized anti-HER1 IgG1 monoclonal antibody (mAb), covalently linked to 2.) a topoisomerase inhibitor, via 3.) a tetrapeptide-based cleavable linker. The antibody is produced in Chinese hamster ovary cells by recombinant DNA technology, and the topoisomerase inhibitor and linker are produced by chemical synthesis. Deruxtecan is composed of a protease-cleavable tetrapeptide linker and the

topoisomerase inhibitor, DXd, which is an exatecan derivative. It is indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received 2 or more prior anti-HER2-based regimens in the metastatic setting. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. The safety and efficacy of Enhertu® were assessed in a single-arm, multicenter study that included female patients (N=184) with HER2-positive, unresectable and/or metastatic breast cancer who had received ≥2 prior anti-HER2 therapies. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. In in a single-arm study, the confirmed objective response rate was 60.3%. In addition, all patients in this study received prior trastuzumab (under the brand name Herceptin® in the US), abo-trastuzumab emtansine (under the brand name Kadcyla® in the US), and 66% had prior pertuzumab (under the brand name Perjeta® in the US). Do not substitute Enhertu® for or with trastuzumab or ado-trastuzumab emtansine.

Recommendation: Enhurtu® to be non-preferred. Add Kanjinti and Ogivri to non-preferred.

Clinical Criteria:

- PA required to confirm FDA approved indication.

Board Decision: The Board unanimously approved the above recommendation.

Esperoct® (antihemophilic factor(recombinant)); **PDL category**- Antihemophilic Agents

Esperoct®, a glycopegylated form of recombinant anti-hemophilic factor, temporarily replaces the missing coagulation Factor VIII needed for effective hemostasis. The Factor VIII in Esperoct® is conjugated to a 40-kDa polyethylene glycol molecule which increases the half-life and decreases the clearance compared to the non-pegylated molecule. It is indicated as a recombinant DNA-derived coagulation Factor VIII concentrate indicated for use in adults and children with hemophilia A for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding
- Routine prophylaxis to reduce the frequency of bleeding episodes

Esperoct® is not indicated for the treatment of von Willebrand disease. The safety and efficacy of Esperoct® were assessed in 5 multinational, open-label trials that included male subjects with severe hemophilia A (<1% endogenous Factor VIII activity). In a clinical trial that included adults and adolescent patients with hemophilia A, 88.4% of bleeds were treated successfully with a single dose in the on-demand arm.

Recommendation: Esperoct® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Eylea® (aflibercept); **PDL category**- OP- Of Interest

Aflibercept, the active ingredient of Eylea®, is a recombinant fusion protein consisting of portions of human vascular endothelial growth factor (VEGF) receptors 1 and 2 extracellular domains fused to the Fc portion of human IgG1. Aflibercept acts as a soluble decoy receptor that binds VEGF-A and PlGF, and

thereby can inhibit the binding and activation of these cognate VEGF receptors. It is indicated for the treatment of: • Neovascular (wet) Age-Related Macular Degeneration (AMD)

- Macular Edema following Retinal Vein Occlusion (RVO)
- Diabetic Macular Edema (DME)
- Diabetic Retinopathy (DR)

The safety and efficacy of Eylea® were assessed in 2 randomized, multicenter, double-masked, active-controlled studies that included patients with wet AMD (N=2412) treated with Eylea® 2mg Q8W following 3 initial monthly doses, Eylea® 2mg Q4W, Eylea® 0.5mg Q4W or ranibizumab 0.5mg Q4W for up to 52 weeks. In a 2018 Cochrane Review by Virgili et al2 that compared anti-VEGR treatments for diabetic macular edema, aflibercept, bevacizumab, and ranibizumab were all more effective than laser for improving vision by 3 or more lines after one year. The ranibizumab group was less likely to gain 3 or more lines of visual acuity at one year compared with aflibercept (RR 0.75, moderate-certainty evidence). For every 1000 people treated with aflibercept, 92 fewer would gain 3 or more lines of visual acuity at one year if treated with ranibizumab. It is not clear if this applies to the long-term. On average people receiving ranibizumab had worse visual acuity at one year (moderate-certainty evidence). Ranibizumab and bevacizumab were comparable with respect to aflibercept and did not differ in terms of visual acuity.). In a clinical study comparing Eylea with the active comparator in patients with wet AMD, Eylea® was found to be as effective as the active comparator for the primary endpoint. With the studies for the other indications, Eylea® was found to be statistically more effective than control (sham) for the primary endpoints assessed.

Recommendation: Eylea® to be non-preferred.

Clinical Criteria:

- Eylea is non-preferred and indicated for the treatment of: Neovascular (wet) Age-Related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR)

Board Decision: The Board unanimously approved the above recommendation.

Givlaari® (givosiran); **PDL category**- Acute Hepatic Porphyria (AHP)

Givosiran, the active ingredient of Givlaari®, is a double-stranded small interfering RNA that causes degradation of aminolevulinate synthase 1 (ALAS1) mRNA in hepatocytes through RNA interference, reducing the elevated levels of liver ALAS1 mRNA. This leads to reduced circulating levels of neurotoxic intermediates aminolevulinic acid (ALA) and porphobilinogen (PBG), factors associated with attacks and other disease manifestations of acute hepatic porphyria. It is indicated for the treatment of adults with acute hepatic porphyria (AHP). The safety and efficacy of Givlaari® were assessed in a multinational, double-blind, randomized, placebo-controlled 6-month duration study that included adults with AHP. Results suggested that on average, AHP patients treated with Givlaari® experienced 70% fewer porphyria attacks as compared with placebo.

Recommendation: Givlaari® to be non-preferred.

Clinical Criteria:

- Add new category Acute Hepatic Porphyria (AHP)
- Givlaari is indicated for the treatment of adults with acute hepatic porphyria (AHP).

Board Decision: The Board unanimously approved the above recommendation.
Gloperba® (colchicine); **PDL category**- Gout

Colchicine, the active ingredient of Gloperba®, is an alkaloid obtained from various species of Colchicum. It is postulated that colchicine works due to its ability to block neutrophil-mediated inflammatory responses induced by monosodium urate crystals in synovial fluid. Colchicine disrupts the polymerization of β-tubulin into microtubules, thus preventing the activation, degranulation, and migration of neutrophils to sites of inflammation. Colchicine also interferes with the inflammasome complex found in neutrophils and monocytes that mediates interleukin-1β (IL-1β) activation. It is indicated for prophylaxis of gout flares in adults. The safety and effectiveness of Gloperba® for acute treatment of gout flares during prophylaxis has not been studied. Gloperba® is not an analgesic medication and should not be used to treat pain from other causes. The evidence for the efficacy of colchicine in patients with chronic gout is derived from published literature. There are 2 studies that assessed the efficacy of colchicine 0.6mg BID for the prophylaxis of gout flares in patients with gout starting treatment with urate-lowering therapy. In both studies, colchicine treatment decreased the frequency of gout flares. Gloperba® is the first liquid formation FDA approved for this indication. This dosage form allows for dose reductions if needed for drug interactions or renal or hepatic impairment. Its safety and efficacy are based on studies with colchicine from published literature.

Recommendation: Gloperba® to be non-preferred.

Clinical Criteria:

- DDI: The concomitant use of Gloperba® and CYP3A4 inhibitors (e.g. clarithromycin, ketoconazole, grapefruit juice, erythromycin, verapamil, etc.) should be avoided due to the potential for serious and life-threatening toxicity.

Board Decision: The Board unanimously approved the above recommendation.

Oxbryta® (voxelotor); **PDL category**- Sickle Cell Disease

Voxelotor, the active ingredient of Oxbryta®, is a hemoglobin S (HbS) polymerization inhibitor that binds to HbS with a 1:1 stoichiometry and has preferential partitioning to red blood cells. By increasing the affinity of Hb for oxygen, voxelotor demonstrates dose-dependent inhibition of HbS polymerization. Non-clinical studies suggest that voxelotor may inhibit RBC sickling, improve RBC deformability, and reduce whole blood viscosity. It is indicated for the treatment of sickle cell disease (SCD) in adults and pediatric patients 12 years of age and older. This indication is approved under accelerated approval based on increase in hemoglobin (Hb). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The safety and efficacy of Oxbryta® in SCD were assessed in a randomized, double-blind, placebo-controlled multicenter study (HOPE) that included patients with 1 to 10 vaso-occlusive crisis (VOC) events within 12 months prior to enrollment and baseline hemoglobin. This indication is approved under accelerated approval based on increase in hemoglobin. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). In one double-blind, placebo-controlled trial, Oxbryta® had a significantly higher Hb response rate as compared with placebo.

Recommendation: Oxbryta® to be non-preferred.

Clinical Criteria:

- For the treatment of patients ≥ 12 years of age.
- DDI: The concomitant use of Oxbryta and strong CYP3A4 inhibitors or fluconazole may increase voxelotor plasma levels and may lead to increased toxicity.

Board Decision: The Board unanimously approved the above recommendation.

Padcev® (enfortumab vedotin); **PDL category**- Cancer

Enfortumab vedotin-ejfv, the active ingredient of Padcev®, is a Nectin-4 directed antibody-drug conjugate (ADC) comprised of a fully human anti-Nectin-4 IgG1 kappa monoclonal antibody conjugated to the small molecule microtubule disrupting agent, monomethyl auristatin E (MMAE). Nectin-4 is an adhesion protein located on the surface of cells. Non-clinical data suggest that the anti-cancer activity of enfortumab vedotin-ejfv is due to the binding of the ADC to Nectin-4-expressing cells, followed by internalization of the ADC-Nectin-4 complex, and the release of MMAE via proteolytic cleavage. Release of MMAE disrupts the microtubule network within the cell, subsequently inducing cell cycle arrest and apoptotic cell death. It is indicated for the treatment of adults with locally advanced or metastatic urothelial cancer (mUC) who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy in the neoadjuvant/adjuvant locally advanced or metastatic setting. This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The safety and efficacy of Padcev® were assessed in a single-arm, multicenter study that included patients with locally advanced or metastatic urothelial cancer who received prior treatment with a PD-1 or PD-L1 inhibitor and platinum-based chemotherapy. This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. In in a single-arm study, the confirmed objective response rate was 44%.

Recommendation: Padcev® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Pretomanid® (pretomanid); **PDL category**- Antimycobacterial/Anti-Tuberculosis

Pretomanid® is an oral nitro-imidazooxazine antimycobacterial drug that kills actively replicating *M. tuberculosis* by inhibiting mycolic acid biosynthesis, thus blocking cell wall production. It is indicated for a limited population: As part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR) or treatment-intolerant or non-responsive multidrug-resistant (MDR) tuberculosis (TB). Approval of this indication is based in limited clinical safety and efficacy data. This drug is indicated for use in a limited and specific population of patients. The safety and efficacy of Pretomanid® were assessed in an open-label study conducted in 3 centers in South Africa in patients with XDR, treatment-intolerant MDR, or non-responsive MDR pulmonary TB, including 51% of the patients who were HIV-positive. The safety and efficacy of Pretomanid® tablets have not been established for its use in combination with drugs other than bedaquiline and linezolid as part of the

recommended dosing regimen. In an open-label study, the treatment success rate was 89%, having a negative culture status at 6 months post treatment.

Recommendation: Pretomanid® to be non-preferred.

Clinical Criteria:

- Pretomanid is indicated as part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR) or treatment-intolerant or non-responsive multidrug-resistant (MDR) tuberculosis (TB). Approval of this indication is based in limited clinical safety and efficacy data. This drug is indicated for use in a limited and specific population of patients.

Board Decision: The Board unanimously approved the above recommendation.

Reblozyl® (luspatercept- aamt); **PDL category**- Anemia-Beta Thalassemia

Luspatercept-aamt, the active ingredient of Reblozyl®, is an erythroid maturation agent. It is a recombinant fusion protein that binds several endogenous TGF-β superfamily ligands, thus diminishing Smad2/3 signaling. It promoted erythroid maturation through differentiation of late-stage erythroid precursors (normoblasts) in mice. In a model of β-thalassemia, luspatercept-aamt decreased abnormally elevated Smad2/3 signaling and improved hematology parameters associated with ineffective erythropoiesis in mice. It is indicated for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions. It is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia. The safety and efficacy of Reblozyl® were assessed in adults with beta thalassemia in a multicenter, randomized, double-blind, placebo-controlled trial that included patients with beta-thalassemia requiring regular RBC transfusions with no transfusion-free period greater than 35 days during that period. Reblozyl® may cause fetal harm when given to a pregnant woman. In the BELIEVE trial, significantly more had a ≥33% reduction from baseline in RBC transfusion burden with a reduction of at least 2 units for 12 consecutive weeks with Reblozyl® as compared with placebo. This is the first FDA approved treatment for patients with this rare blood disorder.

Recommendation: Reblozyl® to be non-preferred.

Clinical Criteria:

- Add new category Anemia-Beta Thalassemia
- Reblozyl is indicated for the the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusion. It is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.

Board Decision: The Board unanimously approved the above recommendation.

Recarbrio® (imipenem anhydrous, cilastatin, and relebactam); **PDL category**- Carbapenems

Recarbrio® is an antibacterial combination product consisting of imipenem (a carbapenem antibacterial), cilastatin (a renal dehydropeptidase inhibitor), and relebactam (a diazabicyclooctane beta lactamase inhibitor). Note that cilastatin limits the renal metabolism of imipenem and does not have antibacterial activity. In addition, relebactam has no intrinsic antibacterial activity. It protects imipenem from

degradation by certain serine beta lactamases. It is indicated in patients 18 years of age and older who have limited or no alternative treatment options for the treatment of:

- Complicated urinary tract infections (cUTI), including pyelonephritis, caused by the following susceptible gram-negative microorganisms: Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae, and Pseudomonas aeruginosa. Approval of this indication is based on limited clinical safety and efficacy data for Recarbrio®.
- Complicated intra-abdominal infections (cIAI) caused by the following susceptible gram-negative microorganisms: Bacteroides caccae, Bacteroides fragilis, Bacteroides ovatus, Bacteroides stercoris, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Fusobacterium nucleatum, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Parabacteroides distasonis, and Pseudomonas aeruginosa. Approval of this indication is based on limited clinical safety and efficacy data for Recarbrio®. To reduce the development of drug-resistant bacteria and maintain the effectiveness of Recarbrio® and other antibacterial agents, Recarbrio® should be used only to treat or prevent infections that proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy. The safety and efficacy of Recarbrio® were supported in part by the previous findings of the efficacy and safety of imipenem/cilastatin (under the brand name Primaxin®) for the treatment of cIAI and cUTI. The contribution of relebactam to Recarbrio® was primarily established in vitro and in animal models of infection. . Its safety and efficacy were in part supported by the previous findings of the efficacy of imipenem/cilastatin (Primaxin®), which has been available for numerous years.

In a 2017 double-blind, randomized, phase 2 dose-ranging study by Sims et al2 that compared the safety and efficacy of imipenem/cilastatin plus relebactam with imipenem/cilastatin alone in patients with cUTIs, high microbiological response rates for both treatments confirmed non-inferiority of imipenem/cilastatin plus relebactam to imipenem/cilastatin alone. The authors concluded that imipenem/cilastatin plus relebactam was as effective as imipenem/cilastatin, while being well tolerated. There is no evidence at this time that Recarbrio® is safer or more effective than the currently preferred medications.

Recommendation: Recarbrio® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Reyvow® (lasmiditan); **PDL category**- Migraine, Misc.

Lasmiditan, the active ingredient of Reyvow®, is a serotonin (5-HT) 1F receptor agonist. While the exact mechanism of lasmiditan is not known, it does bind with high affinity to the 5-HT 1F receptor and it presumably exerts its effects through agonist effects at this receptor. Reyvow® is a Schedule V controlled substance, with abuse potential. It is indicated for the acute treatment of migraine with or without aura in adults. Reyvow® is not indicated for the preventive treatment of migraine. The safety and efficacy of Reyvow® in the acute treatment of migraine were assessed in 2 randomized, double-blind, placebo-controlled trials that included patients with a history of migraine with and without aura per the International Classification of Headache Disorders (ICHD-II) diagnostic criteria.

Recommendation: Reyvow® to be non-preferred.

Clinical Criteria:

- Reyvow is non-preferred and is indicated for the acute treatment of migraine with or without aura in adults. Reyvow® is not indicated for the preventive treatment of migraine.

Board Decision: The Board unanimously approved the above recommendation.

Secuado® (asenapine transdermal system); **PDL category**- Antipsychotics- Atypicals

Asenapine, the active ingredient of Secuado®, is an atypical antipsychotic. While the mechanism of action for its approved indication is not clear, it is thought its efficacy could be mediated through a combination of antagonist activity at D2 and 5-HT2A receptors. It is indicated for the treatment of adults with schizophrenia. Secuado® has a box warning regarding the increased mortality in elderly patients with dementia-related psychosis. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Secuado® is not approved for the treatment of patients with dementia-related psychosis. The efficacy of Secuado® was established, in part, on the basis of efficacy data from trials with the sublingual formulation of asenapine, available as brand name Saphris®. In addition, a 6-week, fixed-dose, randomized, double-blind and placebo-controlled trials assessed the safety and efficacy of Secuado® that included adult patients who met DSM-IV criteria for schizophrenia. . In a short-term clinical trial compared with placebo, Secuado® was statistically significantly superior to placebo for improvement in PANSS total score and CGI-S. Secuado® is the first and only FDA-approved transdermal system for schizophrenia, thus providing a new dosage formulation option for treating physicians.

Recommendation: Secuado® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Tazverik® (tazemetostat); **PDL category**- Cancer

Tazemetostat, the active ingredient of Tazverik®, is an inhibitor of the methyltransferase, EZH2, and some EZH2 gain-of-function mutations. Tazemetostat also inhibited EZH1. It is indicated for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection. 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 efficacy of Tazverik® was assessed in an open-label, single-arm cohort (Cohort 5) of a multicenter study that included patients with histologically confirmed, metastatic or locally advanced epithelioid sarcoma.
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. Tazverik® is the first and only FDA-approved EZH2 inhibitor, as well as the first and only FDA-approved treatment specifically for patients with epithelioid sarcoma. In a small open-label study, Tazverik® produced a 15% overall response rate.

Recommendation: Tazverik® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Tepezza® (teprotumumab-trbw); **PDL category**- Thyroid Eye Disease

Teprotumumab-trbw, the active ingredient of Tepezza®, is an insulin-like growth factor-1 receptor inhibitor (IGF-1R). It is a fully human IgG1 monoclonal antibody produced in Chinese hamster ovary cells. Its mechanism of action has not been fully characterized, but teprotumumab-trbw binds to IGF-1R and blocks its activation and signaling.

Recommendation: Tovet® Foam be non-preferred.

Clinical Criteria:

- For the treatment of patients ≥ 12 years of age.

Board Decision: The Board unanimously approved the above recommendation.

Tepezza® (teprotumumab-trbw); **PDL category**- Thyroid Eye Disease

Teprotumumab-trbw, the active ingredient of Tepezza®, is an insulin-like growth factor-1 receptor inhibitor (IGF-1R). It is a fully human IgG1 monoclonal antibody produced in Chinese hamster ovary cells. Its mechanism of action has not been fully characterized, but teprotumumab-trbw binds to IGF-1R and blocks its activation and signaling. It is indicated treatment of Thyroid Eye Disease. The safety and efficacy of Tepezza® were assessed in 2 randomized, double-masked, placebo-controlled studies that included patients with Thyroid Eye Disease. In 2 clinical trials, Tepezza® improved proptosis responder rates as compared with placebo.

Recommendation: Tepezza® to be non-preferred.

Clinical Criteria:

- Add new category Thyroid Eye Disease.

Board Decision: The Board unanimously approved the above recommendation.

Ubrelvy® (ubrogepant); **PDL category**- Migraine, Misc

Ubrogepant, the active ingredient of Ubrelvy®, is a small molecule calcitonin gene-related peptide (CGRP) receptor antagonist. It is indicated for the acute treatment of migraine with or without aura in adults. This is not indicated for the preventive treatment of migraine. The safety and efficacy of Ubrelvy® for the acute treatment of migraine were assessed in 2 randomized, double-blind, placebo-controlled trials. In both studies, patients were instructed to treat a migraine with moderate to severe headache pain intensity; a second dose of study medication, or the patient's usual acute treatment for migraine, was permitted between 2 to 48 hours after the initial treatment for a non-responding or recurrent migraine headache. In 2 clinical trials compared with placebo, Ubrelvy® significantly increased the proportion of patients achieving headache pain freedom and most bothersome symptom freedom at 2 hours post-dose.

Recommendation: Ubrelvy® to be non-preferred.

Clinical Criteria:

- Ubrelvy is non-preferred and is indicated for the acute treatment of migraine with or without aura in adults. This is not indicated for the preventive treatment of migraine.

Board Decision: The Board unanimously approved the above recommendation.

Vumerity® (diroximel fumarate); **PDL category**- Multiple Sclerosis, Non-Interferons

The mechanism by which diroximel fumarate, the active ingredient of Vumerity®, exerts its therapeutic effect in multiple sclerosis is not known. Monomethyl fumarate (MMF) is the active metabolite of diroximel fumarate, and it has been shown to activate the nuclear factor (erythroid-derived 2)- like 2 (Nrf2) pathway. The Nrf2 pathway is involved in the cellular response to oxidative stress. After oral administration of Vumerity®, diroximel fumarate undergoes rapid pre-systemic hydrolysis by esterases and is converted to its active metabolite, monomethyl fumarate (MMF). Diroximel fumarate is not quantifiable in plasma after oral administration of Vumerity®. 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. The efficacy of Vumerity® is based upon bioavailability studies in patients with relapsing forms of MS and healthy subjects comparing oral dimethyl fumarate delayed-release capsules to Vumerity® delayed-release capsules. The authors concluded in one phase 3 study3 that diroximel fumarate had an improved GI tolerability profile as compared with dimethyl fumarate, as there were lower rates of gastrointestinal adverse events seen with diroximel fumarate than dimethyl fumarate. In addition, there were fewer patients who discontinued treatment with diroximel fumarate as compared with dimethyl fumarate due to adverse events and fewer who discontinued due to gastrointestinal adverse events. There is some evidence at this time to support that Vumerity® may have better gastrointestinal tolerability as compared to dimethyl fumarate; however, there is no evidence at this time to support that Vumerity® is safer or more effective than the other currently available, more cost-effective medications.

Recommendation: Vumerity® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Vyondys® 53 (golodirsen); **PDL category**- Muscular Dystrophy Agents

Golodirsen, the active ingredient of Vyondys® 53, is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass. It is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping. It is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Vyondys® 53. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials. This is the second RNA exon-skipping agent by Sarepta Therapeutics. The mean changes in dystrophin levels significantly increased from normal levels with Vyondys® 53 by 48 weeks of treatment. A placebo-controlled, post-marketing confirmatory trial to support accelerated approval, the ESSENCE study, is currently enrolling and expected to conclude by 2024.

Recommendation: Vyondys® 53 to be non-preferred.

Clinical Criteria:

- Vyondys® 53: • The prescriber is, or has consulted with, a neuromuscular disorder specialist AND • The dose does not exceed 30mg/kg once weekly AND • The patient is currently on a stable corticosteroid dose for at least 6 months. • The patient must be ambulatory (able to walk with or without assistance, not wheelchair bound).
- Note: Initial approval will be granted for 6 months. For re-approval after 6 months, the patient must demonstrate a response to therapy as evidenced by remaining ambulatory (able to walk with or without assistance, not wheelchair bound).

Board Decision: The Board unanimously approved the above recommendation.

Wakix® (pitolisant); **PDL category**- Stimulant- Stimulant Like

Pitolisant, the active ingredient of Wakix®, is an antagonist/inverse agonist of the histamine-3 (H3) receptor. It's mechanism of action when used for its approved indication is not clear; however, its efficacy could be mediated through its activity as an antagonist/inverse agonist at histamine-3 (H3) receptors. It is indicated for the treatment of excessive daytime sleepiness (EDS) in adults with narcolepsy. The safety and efficacy of Wakix® for the treatment of excessive daytime sleepiness in adults with narcolepsy were assessed in 2 multicenter, randomized, double-blind, placebo-controlled studies that included adults who met the International Classification of Sleep Disorders (ICSD-2) criteria for narcolepsy and who had an Epworth Sleepiness Scale (ESS) score ≥14. In 2 clinical trials compared with placebo, Wakix® demonstrated statistically significantly greater improvement on the primary endpoint, the least square mean final ESS score. There is no evidence at this time that Wakix® is safer or more effective than the currently preferred medications.

Recommendation: Wakix® to be non-preferred.

Clinical Criteria:

- Wakix is non-preferred and is indicated for the treatment of excessive daytime sleepiness (EDS) in adults with narcolepsy

Board Decision: The Board unanimously approved the above recommendation.

Zolgensma® (onasemnogene abeparvovec- xioi); **PDL category**- Neurologics- SMA

Zolgensma® is a suspension of an adeno-associated viral vector-based gene therapy that is a recombinant self-complementary AAV9 containing a transgene encoding the human survival motor neuron (SMN) protein, under the control of a cytomegalovirus enhancer/chicken-β-actin hybrid promoter. It is a recombinant AAV9-based gene therapy designed to deliver a copy of the gene encoding the human SMN protein. Spinal muscular atrophy is caused by a bi-allelic mutation in the *SMN1* gene, which results in insufficient SMN protein expression. It is indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1* (*SMN1*) gene. The safety and efficacy of repeat administration of Zolgensma® have not been evaluated. The use of Zolgensma® in patients with advanced SMA (e.g. complete paralysis of limbs, permanent ventilator-dependence) has not been evaluated. The safety and efficacy of Zolgensma® were assessed in an open-label, single-arm clinical trial (ongoing) and an open-label, single-arm, ascending dose clinical trial

(completed) that included pediatric patients less than 2 years of age with SMA with bi-allelic mutations in the SMN1 gene. Patients experienced onset of clinical symptoms consistent with SMA before 6 months of age. The safety and efficacy of repeat administration of Zolgensma® have not been evaluated. The use of Zolgensma® in patients with advanced SMA has not been evaluated. Zolgensma® has a box warning regarding acute serious liver injury.

Recommendation: Zolgensma® to be non-preferred.

Clinical Criteria:

- The patient is less than 2 years of age AND The diagnosis is spinal muscular atrophy (SMA) AND The patient has bi-allelic mutations of the SMN1 gene AND The patient does not have advanced SMA (e.g. complete paralysis of limbs or permanent ventilator dependence) AND Medication is prescribed per the dosing guidelines in the package insert (recommended dose is 1.1 x 104 vector genomes per kilogram) AND Baseline anti-AAV9 antibodies are less than 1:50 Prior to starting therapy and periodically for at least 3 months, the following laboratory tests will be conducted: Liver function (AST, ALT, total bilirubin, prothrombin time), platelet counts, and troponin-I
- Note: The safety and effectiveness of repeat administration has not been evaluated. Approval is limited to a single intravenous infusion.

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

FDA warns about serious breathing problems with seizure and nerve pain medicines gabapentin (Neurontin, Gralise, Horizant) and pregabalin (Lyrica, Lyrica CR)
https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-serious-breathing-problems-seizure-and-nerve-pain-medicines-gabapentin-neurontin?utm_campaign=FDA%20MedWatch%20-%20gabapentin%20and%20pregabalin%29%3A%20Drug%20Safety%20Communication&utm_medium=email&utm_source=Eloqua

INVIRASE: pregnancy and lactation label updates
http://s2027422842.t.en25.com/e/es?s=2027422842&e=286692&elqTrackId=376c7bc788024cd5a73d955f2e3dcbdc&elq=4e689a40467c423291cd63c181b0c7b6&elqaid=10694&elqat=1

KALETRA and NORVIR: drug-drug interaction updates
http://s2027422842.t.en25.com/e/es?s=2027422842&e=286712&elqTrackId=376c7bc788024cd5a73d955f2e3dcbdc&elq=ae9e9ecc8df44044bd83dd763895863b&elqaid=10697&elqat=1

FDA requests withdrawal of bacitracin for injection from market
https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-withdrawal-bacitracin-injection-market?utm_campaign=FDA%20requests%20withdrawal%20of%20bacitracin%20for%20injection%20from%20market&utm_medium=email&utm_source=Eloqua

FDA launches mobile-friendly database with information on life-saving HIV drugs as part of ongoing mission to empower the public through increased access to information and data
https://www.fda.gov/news-events/press-announcements/fda-launches-mobile-friendly-database-information-life-saving-hiv-drugs-part-ongoing-mission-

empower?utm_campaign=FDA%20launches%20mobile-friendly%20database%20with%20information%20on%20life-saving%20HIV%20drugs&utm_medium=email&utm_source=Eloqua

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

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **June 16, 2020** 5:30pm –8:30pm at the Augusta Armory.