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: 12/16/2019
RE: Maine DUR Board **Meeting** minutes from December 10, 2019

ATTENDANCE	PRESENT	ABSENT	EXCUSED
Linda Glass, MD			X
Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR	X		
Mike Antoniello, MD			X
Kathleen Polonchek, MD	X		
Kenneth McCall, PharmD			X
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

Stefanie Diloreto from MaineMed: Highlighted the attributes of Trikafta.
Melissa Mattice from Vertex: Highlighted the attributes of Trikafta.
Nicole Trask from J&J: Highlighted the attributes of Spravato.
Gene Muisa from Amgen: Highlighted the attributes of a Biosimilas.
Frank Nagy from Xeris: Highlighted the attributes of Gvoke.

OLD BUSINESS

DUR MINUTES

The October DUR meeting minutes were accepted after a couple minor spelling corrections.

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE

No update at this time.

REVISED CLINICAL CRITERIA/PREFERRED REVIEW

Antidepressants - Selected SSRI's Criteria:
Conscious Sedation as defined be the following:
1. Pre-procedure patient evaluation and preparation
    - Medical records review
    - Underlying medical issues
    - Preparation of the patient
    - Pre-procedure instruction, medication usage, counseling, fasting
2. Patient Monitoring
    - Level of consciousness (responsiveness)
    - Breathing/ventilation
    - Oxygenation
    - Pulse oximetry-continuous monitoring with alarm capability
    - Hemodynamic monitoring
    - Contemporaneous recording of at least HR and oximetry with frequent BP monitoring that is automated or individual able to measure BP frequently (e.g. every 5-10 min) during period of sedation.
    - Presence of individual dedicated to patient monitoring during period of sedation
3. Supplemental oxygen available
4. Emergency support
    - Presence of individual(s) capable of establishing a patent airway (i.e. advanced life-support skills)
    - Presence of emergency and airway equipment
    - Includes suction, airway adjunct such as bag-valve mask and oral and nasal airways
    - Presence of individual to establish intravenous access
5. Recovery Care
    - Observe and monitor patients in appropriately staffed and equipped area until near baseline level of consciousness and are no longer at risk for cardiorespiratory depression
    - Monitor oxygenation continuously until patients are no longer at risk for hypoxemia.
    - Monitor ventilation and circulation at regular intervals
    - Design discharge criteria to minimize risk of CNS or cardiorespiratory depression after discharge from observation by trained personnel

Board Decision: The Board unanimously approved the above recommendation.

Toujeo® (Insulin Glargine); **PDL category-** Diabetic- Penfills

Recommendation: Stay non-preferred for 1/1/20

Board Decision: The Board unanimously approved the above recommendation.

REVISED CLINICAL CRITERIA

Spinraza®(nusinersen)**; PDL category-** Neurologics- SMA

Recommendation:

Clinical criteria:

The diagnosis is spinal muscular atrophy (SMA) type 1, 2, or 3 (results of genetic testing must be submitted) AND The patient has at least 2 copies of the SMN2 gene AND The prescriber is a neurologist, pulmonologist, or other physician with expertise in treating SMA ~~AND The need for invasive or noninvasive ventilation (if applicable) does not exceed more than 6 hours per 24-hour period AND~~ Baseline motor ability has been established using one of the following exams:
Hammersmith Infant Neurological Exam (HINE)
Hammersmith Functional Motor Scale Expanded (HFMSE)
Upper Limb Module Test (non-ambulatory)
Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) AND
Prior to starting therapy, and prior to each dose, the following laboratory tests will be conducted:

- Treating provider attests the member has a platelet count > 50,000/ml or greater
- Treating provider agrees to do platelet count and coagulation test before each dose
- Treating provider agrees to do a quantitative spot urine protein test before each dose

Concomitant use of Spinraza and Zolgensma is investigational and will not be approved AND Use of Spinraza after gene replacement therapy, including Zolgensma is investigational and will not be approved. ~~Platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), and quantitative spot urine protein~~
Note: Initial approval will be granted for 4 loading doses (the first 3 loading doses should be administered at 14-day intervals; the 4th loading dose should be administered 30 days after the 3rd dose). Renewal may be granted for up to 12 months with a maximum of 3 doses approved per year (12mg (5ml) every 4 months). For therapy continuation, clinical documentation must be submitted documenting improvement or maintenance of motor ability OR slower progression of disease than would otherwise be expected.

Board Decision: The Board unanimously approved the above recommendation.

Biosimilars

Mvasi® (bevacizumab- awwb**); PDL category-** Cancer

Recommendation: Mvasi® be non-preferred.

Kanjinti® (trastuzumab-anns)**; PDL category-** Antineoplastics- Monoclonal Antibodies

Recommendation: Kanjinti® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

NEW BUSINESS

DATA PRESENTATION: APPROPRIATE USE OF ASTHMA CONTROLLER MEDICATIONS

The National Heart, Lung and Blood Institute has published Guidelines for the Diagnosis and Management of Asthma. The treatment of asthma is done in a step-wise manner, and depending on disease severity, a combination of several agents may be needed. For anyone who requires use of a short acting agent ≥ 2 days/week, a controller medication daily is recommended. The Guidelines state that the frequency of short acting beta-adrenergic inhaler (SABA) use can be clinically useful as a measure of disease activity since increased use of a SABA has been associated with increased risk for death or near death in patients who have asthma. Use of more than one SABA canister every one to two months is also associated with an increased risk of an acute exacerbation. Therefore, the use of more than one SABA canister (e.g., albuterol 200 puffs per canister) during a one-month period most likely indicates over reliance on this drug and suggests inadequate control of asthma. Additionally, inhaled corticosteroids (ICS) are the preferred long-term control therapy in asthma for all ages, although leukotriene receptor antagonists (LTRA) are listed as an alternative. Long-acting beta-adrenergic inhalers (LABAs) should never be used without first using ICS inhalers due to the increased risk of asthma exacerbations and death.

We will use paid, non-reversed Medicaid pharmacy claims from January 2018 through December 2018, excluding members with Part D, MaineRX and TPL. Change Healthcare will review paid non-reversed pharmacy and medical claims with dates of service from 1/1/2018 through 12/31/2018, excluding members who had a diagnosis of cystic fibrosis, COPD or emphysema. Members will be stratified by age and the number of short acting inhalers used per year. In addition, the number of members in each group who had an ER visit or hospitalization associated with an asthma diagnosis during the study period will be reported. We will compare the rates of ER visits and hospitalizations to the rates seen in the 2015 analysis, examining whether the educational interventions provided by the Board had an impact in reducing rates of asthma exacerbations, understanding that the populations are not identical. Additional analysis will be done on those using more than 12 short acting inhalers/year and sorted geographically. The prescribers for these members will be identified to look at providers who are possibly practicing outside of guideline recommendations, perhaps identifying those who would be appropriate for more targeted education.

Recommendation: For the providers who prescribed more than 12 short-acting inhalers/year for individual members, see how many of those members were also on a long-acting controller medication, such as a corticosteroid inhaler and/or leukotriene antagonist. Another strategy would be to contact providers who had very high numbers of prescriptions/year (over 20) to investigate the reasons for need for so many short-acting inhalers. IN the cases where there were between 13 and 16 inhalers dispensed, some could have been so that the member could have inhalers kept in different locations, such as with school nurses, at work, etc. it is hard to assume that each of the dispensed inhalers were used completely within a given month.

Board Decision: The Board unanimously approved the above recommendation.

DATA PRESENTATION: USE OF STATINS IN MEMBERS WITH DIABETES MELLITUS

Will be brought back to next meeting

Board Decision: No action needed at this time.

NEW DRUG REVIEW

Adhansia® (methylphenidate extended- release); **PDL category-** Stimulant-Methylphenidate, Long-acting

Methylphenidate, the active ingredient of Adhansia® XR, is a central nervous system (CNS) stimulant. The exact mode of action in ADHD is not known. Methylphenidate blocks the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extra neuronal space. Adhansia® XR capsules contain multilayered beads, composed of an immediate-release layer which contains about 20% of the dose and a controlled-release layer which contains about 80% of the methylphenidate dose. Adhansia® XR is a Schedule II controlled substance. It is to be taken once daily in the morning. It is indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in patients 6 years and older. The safety and efficacy of Adhansia® XR were established in two randomized double-blind placebo-controlled trials in adults, as well as in 2 pediatric trials. Some, but not all doses were found to be significantly more effective than placebo in clinical trials assessing efficacy, based on average PERMP and SKAMP scores, as well as ADHD-RS-IV scores. There is no evidence at this time that Adhansia® XR is safer or more effective than the currently preferred medications.

Recommendation: Adhansia® be non-preferred.

Clinical Criteria:

- Non-preferred products must be used in specified step order.
- For the treatment of patients ≥ 6 years of age.

Board Decision: The Board unanimously approved the above recommendation.

Aklief® (trifarotene); **PDL category-** Topical-Acne Preparations

Trifarotene, the active ingredient of Aklief®, is a terphenyl acid derivative and is a retinoid. It is an agonist of retinoic acid receptors (RAR), with particular activity at the gamma subtype of RAR. Stimulation of RAR results in modulation of target genes, which are associated with various processes, including cell differentiation and mediation of inflammation. The exact mechanism of action by which trifarotene works for acne is not known. It is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older. The safety and efficacy of use of Aklief® cream in the treatment of moderate facial and truncal acne vulgaris were assessed in 2 randomized, multicenter, parallel group, double-blind, vehicle-controlled trials of identical design. Per the full-text study by Tan et al[2], the facial and truncal success rates per the IGA and PGA, respectively, as well as the changes in inflammatory and non-inflammatory lesion counts were all significantly ($p<0.001$) in favor of trifarotene when compared with vehicle. In a long-term 52-week study by Blune-Peytavi et al[3], trifarotene was found to be safe, well-tolerated, and effective in moderate facial and truncal acne. There is no evidence at this time that Aklief® cream is safer or more effective than the currently preferred medications.

Recommendation: Aklief®will be non-preferred.

Clinical Criteria:

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

Board Decision: The Board unanimously approved the above recommendation.

Beser® Lotion (fluticasone propionate); **PDL category**- Topical-Corticosteroids, Medium Potency

Fluticasone propionate, the active ingredient of Beser® lotion, is a synthetic fluorinated corticosteroid. Corticosteroids play a role in cellular signaling, immune function, inflammation, and protein regulation; however, the exact mechanism of action in atopic dermatitis is not known. Studies performed with fluticasone propionate lotion, 0.05% indicate that it is in the medium range of potency per vasoconstrictor trials in healthy subjects when compared with other topical corticosteroids. However, similar blanching scores do not necessarily imply therapeutic equivalence. It is indicated for the relief of the inflammatory and pruritic manifestations of atopic dermatitis in patients 3 months of age or older. In clinical trials, fluticasone propionate lotion was found to be superior to vehicle in the treatment of atopic dermatitis. Fluticasone lotion 0.05% generic and brand name Cutivate® have been available for several years. The clinical trials included for Beser® lotion were the same as those in the Cutivate® lotion clinical trials section of the prescribing information. Both are given once daily with the same indication.

Recommendation: Beser® Lotion be non-preferred.

Clinical Criteria:

- At least 1 drug from each potency of preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Drizalma® Sprinkle (duloxetine capsule, delayed release); **PDL category**- Antidepressants, Selected SSRIs

Duloxetine, the active ingredient of Drizalma® Sprinkle, is a selective serotonin and norepinephrine reuptake inhibitor (SNRI). While the exact mechanisms of the antidepressant, central pain inhibitory and anxiolytic actions of duloxetine in humans are not known, these actions are believed to be related to its potentiation of serotonergic and noradrenergic activity in the CNS. It is indicated for the treatment of Major Depressive Disorder (MDD) in adults, Generalized Anxiety Disorder (GAD) in adults and pediatric patients 7 years to 17 years old, Diabetic Peripheral Neuropathy (DPN) in adults. For the management of Chronic Musculoskeletal pain in adults. The prescribing information for Drizalma® Sprinkle had the same studies included as Cymbalta®, a brand name duloxetine extended-release capsule, with the exception of fibromyalgia. Cymbalta® has been on the market for numerous years and has a generic version as well. It was been found to be safe and effective. While Drizalma® Sprinkle has the same doses of Cymbalta®, Drizalma® is available in an additional dose of 40mg. In addition, Drizalma® Sprinkles may be opened and the contents sprinkled over applesauce or added for nasogastric tube administration. This is unlike Cymbalta®, where the capsules should not be opened. Efficacy studies were those from the Cymbalta® clinical trials, another duloxetine extended-release capsule formulation. Drizalma® Sprinkles, however, can be opened and the contents sprinkled on applesauce or administered in a nasogastric tube. There is

no evidence at this time that Drizalma® Sprinkle is safer or more effective than the currently preferred medications.

Recommendation: Drizalma® Sprinkles be non-preferred.

Clinical Criteria:

- Preferred drugs (including failure of at least one preferred SSRI, one SNRI and one non-SSRI/SNRI) must be tried for at least 4 weeks each 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.

Duaklir® Pressair (aclidinium bromide and formaterol fumarate); **PDL category**- Antiasthmatic-Adrenergic Anticholinergic

Duaklir® Pressair is a combination inhaler for oral inhalation that includes aclidinium bromide (an anticholinergic with specificity for muscarinic receptors) and formoterol fumarate (a selective beta2-adrenergic agonist). Aclidinium is a long-acting antimuscarinic agent, also known as an anticholinergic, that exerts its pharmacological effects through inhibition of M3 receptors at the smooth muscle leading to bronchodilation. Formoterol is a long-acting selective beta2-adrenergic agonist, also known as a LABA, that acts locally in the lung as a bronchodilator. It is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Duaklir® Pressair is not indicated for the relief of acute bronchospasm or for the treatment of asthma. The safety and efficacy of Duaklir® Pressair were assessed in a clinical development program that included 3 dose-ranging trials, one active and two placebo-controlled lung function trials of 24 weeks in duration, and one 28-week long-term safety extension study. There is some evidence at this time to suggest that Duaklir® Pressair is more effective than tiotropium for the endpoint of improved 1-hour post-dose FEV; however, there is no evidence to suggest it is safer or more effective than the other currently preferred medications.

Recommendation: Duaklir® Pressair be non-preferred.

Clinical Criteria:

- Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists. Duoneb components are available separately without PA.

Board Decision: The Board unanimously approved the above recommendation.

Ezallor® Sprinkle (rosuvastatin capsule); **PDL category**- Cholesterol- HGM-CoA & Absorb Inhibitors More Potent Drugs/Combos

Rosuvastatin, the active ingredient of Ezallor® Sprinkle, is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methyglutaryl coenzyme A to mevalonate, a precursor of cholesterol. It is indicated for Hypertriglyceridemia- as adjunctive therapy to diet, Primary Dysbetalipoproteinemia (Type III Hyperlipoproteinemia)- as adjunct to diet, Adult Patients with Homozygous Familial Hypercholesterolemia (HFH)- as adjunctive therapy to other lipid-lowering treatments (e.g. LDL apheresis) or alone if such treatments are unavailable to reduce LDL-C, Total-C and ApoB in adults with HFH. Note that pediatric use information for patients 7 to 17 years of age is approved for AstraZeneca's Crestor® (rosuvastatin calcium) tablets. However, due to AstraZeneca's marketing exclusivity rights, this drug product is not labeled with that pediatric information. Ezallor® Sprinkle has not been studied in Frederickson Type 1 and V dyslipidemias. The safety and efficacy of Ezallor® Sprinkle were based on the efficacy of rosuvastatin calcium tablets (brand name Crestor®). Both brand and generic Crestor® tablets have been found to be safe and effective and have been available for numerous years. Ezallor® offers providers the availability of a new dosage form and the capsules can be opened for ease of administration for patients who cannot swallow.

Recommendation: Ezallor® be non-preferred.

Clinical Criteria:

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

Board Decision: The Board unanimously approved the above recommendation.

Fasenra® Pen (benralizumab); **PDL category**- Antiasthmatic- Anti-inflammatory Agents

Benralizumab, the active ingredient of Fasenra®, is a humanized afucosylated, monoclonal antibody (IgG1, kappa) that directly binds to the alpha subunit of the human interleukin-5 receptor (IL-5Rα). The IL-5 receptor is expressed on the surface of eosinophils and basophils. Benralizumab, by binding to the IL-5Rα chain, reduces eosinophils through antibody-dependent cell-mediated cytotoxicity (ADCC); however, the mechanism of action in asthma has not been definitively established. It is indicated as the add on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype. Fasenra® is not indicated for treatment of other eosinophilic conditions and is not indicated for the relief of acute bronchospasm or status asthmaticus. Several studies were performed to assess the safety and efficacy of Fasenra®, including one 52-week dose ranging exacerbation trial, 3 confirmatory trials, and one 12-week lung function trial. Fasenra® is intended for use under the guidance of a healthcare provider; however, Fasenra® pen (auto-injector) is now available and is intended for administration by patients or caregivers. Patients or caregivers may inject after proper training in subcutaneous injection technique. The prefilled syringe is for administration by a healthcare provider. Fasenra® was found in clinical trials to be effective for having a lower rate of asthma exacerbation as compared with placebo and it also provided consistent improvements over time in the mean change from baseline in FEV1. Subgroup analyses did find patients with a higher prior exacerbation history and baseline blood eosinophil count as potential predictors of improved treatment response.

Recommendation: Fasenra® Pen be non-preferred.

Clinical Criteria:

- For patients with severe asthma aged 12 years or older and eosinophilia.

- Fasenra, Nucala and Cinqair are not indicated for treatment of other eosinophilic conditions and are not indicated for the relief of acute bronchospasm or status asthmaticus.
- Fasenra: For the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.

Board Decision: The Board unanimously approved the above recommendation.

Gvoke® (glucagon injection); **PDL category**- Glucose Elevating Agents

Glucagon, the active ingredient of Gvoke®, is an anti-hypoglycemic agent that is identical to human glucagon. Glucagon increases blood glucose concentration by activating hepatic glucagon receptors, thus stimulating glycogen breakdown and release of glucose from the liver. Hepatic stores of glycogen are necessary for glucagon to produce an anti-hypoglycemic effect. It is indicated for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages 2 years and above. The safety and efficacy of Gvoke® were assessed in 2 multicenter, 2-way crossover studies in adult patients aged 18 to 74 years of age with type 1 diabetes. In clinical trials, Gvoke® was non-inferior to glucagon emergency kit administration in adults with type 1 diabetes regarding treatment success. In a pediatric clinical trial, patients underwent insulin-induced hypoglycemia and achieved a target glucose increase of at least 25mg/dl. There is no evidence at this time that Gvoke® is safer or more effective than the currently preferred medications.

Recommendation: Gvoke® be non-preferred.

Clinical Criteria:

- For the treatment of patients ≥ 2 years of age.

Board Decision: The Board unanimously approved the above recommendation.

Inrebic® (fedratinib); **PDL category**- Cancer

Fedratinib, the active ingredient of Inrebic®, is a kinase inhibitor with activity against wild type and mutationally activated Janus Associated Kinase 2 (JAK2) and FMS-like tyrosine kinase 3 (FLT3). It is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF). The safety and efficacy of Inrebic® were assessed in a double-blind, randomized, placebo-controlled trial (JAKARTA) that included patients with intermediate-2 or high-risk myelofibrosis (MF), post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis with splenomegaly. In a clinical trial, a significantly larger percent of patients in the Inrebic® group had spleen volume reduction by 35% or more as compared with placebo.

Recommendation: Inrebic® be non-preferred.

Clinical Criteria:

- Inrebic will be considered for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF)

Board Decision: The Board unanimously approved the above recommendation.

Katerzia® (amlodipine); **PDL category**- Calcium Channel Blockers

Amlodipine benzoate, the active ingredient of Katerzia®, is a long-acting calcium channel blocker. It is a dihydropyridine calcium antagonist (calcium ion antagonist or slow-channel blocker) that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extracellular calcium ions into these cells through specific ion channels. Amlodipine inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells. It is indicated for the treatment of: Hypertension, Coronary Artery Disease (CAD): For the symptomatic treatment of chronic stable angina. May be used alone or in combination with other antianginal agents, For the treatment of confirmed or suspected vasospastic angina (Prinzmetal's or Variant Angina). May be used as monotherapy or in combination with other antianginal agents, In patients with recently documented CAD by angiography and without heart failure or an ejection fraction <40%, it is indicated to reduce the risk of hospitalization for angina and to reduce the risk of a coronary revascularization procedure. Amlodipine tablets (under brand name Norvasc®) have been FDA approved for numerous years and have been found to be safe and effective. The exposure (Cmax and AUC) of Katerzia® oral suspension is similar to that of Norvasc® tablets. Katerzia® oral suspension has the same indications as amlodipine tablets and the same clinical trials in the prescribing information as amlodipine tablets. It is the first and only FDA approved amlodipine oral suspension. There is no evidence at this time that Katerzia® is safer or more effective than the currently preferred, more cost-effective medications.

Recommendation: Katerzia® be non-preferred.

Clinical Criteria:

- Preferred drugs must be tried and failed (in step-order) due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Minolira® ER (minocycline, extended-release); **PDL category**- Tetracyclines

Minocycline, the active ingredient of Minolira®, is a semi synthetic derivative of tetracycline. The mechanism of action for its indication is not known. It is indicated to treat the inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 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, Minolira® should be used only as indicated. The safety and efficacy of minocycline ER tablets were assessed in two 12-week, multicenter, randomized, double-blind placebo-controlled trials that included subjects 12 years of age and older. The mean age of included subjects was 20 years, while most were white (73%). Subjects in the two 2 trials (N=924) were randomized to minocycline ER or placebo for 12 weeks. 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, Minolira® should be used only as indicated. Minocycline ER tabs were found to be more effective in 2 clinical trials compared to placebo for its primary endpoints. These clinical trials were the same clinical trials found in the Solodyn® prescribing information, another minocycline ER tablet version with the same indication as Minolira®. Solodyn® has a generic version available.
Recommendation: Minolira® ER be non-preferred.

Clinical Criteria:

- Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Nayzilam® (midazolam spray); **PDL category**- Anticonvulsants

Midazolam, the active ingredient of Nayzilam®, is a compound of the benzodiazepine class. The exact mechanism of action for midazolam is not fully understood, but it is thought to involve potentiation of GABAergic neurotransmission resulting from binding at the benzodiazepine site of the GABA-A receptor. It is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e. seizure clusters, active repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older. The safety and efficacy of Nayzilam® for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e. seizure clusters, active repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy were established in a randomized, double-blind, placebo-controlled study. It carries a box warning regarding increased risks from concomitant use with opioids. In a clinical study compared with placebo, a statistically significant greater number in the Nayzilam® group met the primary endpoint of treatment success. Nayzilam® is not recommended for chronic, daily use as an anticonvulsant because of the potential for development of tolerance to midazolam. It is recommended that Nayzilam® be used to treat no more than one episode every 3 days and no more than 5 episodes per month.

Recommendation: Nayzilam® be non-preferred.

Clinical Criteria:

- Quantity limit. 5/month.

Board Decision: The Board unanimously approved the above recommendation.

Nourianz® (istradefylline); **PDL category**- Parkinson's- Adensine Receptor Antagonist

Istradefylline, the active ingredient of Nourianz®, is an adenosine receptor antagonist, which has a xanthine derivative structure. The mechanism of action by which it exerts its therapeutic effects in Parkinson disease is not known. In *in vitro* and *in vivo* animal studies, istradefylline was demonstrated to be an adenosine A2A receptor antagonist. It is indicated as an adjunctive treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "off" episodes. The

safety and efficacy of Nourianz® for the adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes was shown in 4 randomized, multicenter, double-blind, placebo-controlled, 12-week studies. In clinical trials compared with placebo, patients treated with Nourianz® experienced a statistically significant decrease from baseline in percentage of daily awake "off" time.
Recommendation: Nourianz® be non-preferred.

Clinical Criteria:

- DDI: Avoid use of Nourianz® with strong CYP3A4 inducers (e.g. carbamazepine, rifampin, phenytoin, St. John's wort).

Board Decision: The Board unanimously approved the above recommendation.

ProAir® Digihaler (albuterol sulfate); **PDL category**- Anti-asthmatic- Beta Adrenergic

Albuterol sulfate, the active ingredient of ProAir® Digihaler, is a beta2-adrenergic agonist. Its effects are attributable to activation of beta2-adrenergic receptors on airway smooth muscle. Albuterol relaxes the smooth muscle of all airways, from trachea to the terminal bronchioles. It is indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease. The prevention of exercise-induced bronchospasm in patients 4 years of age and older. The safety and efficacy of ProAir® Digihaler has been established in the treatment and prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease, as well as in the prevention of exercise-induced bronchospasms in patients 4 years of age and older. The use of ProAir® Digihaler for these indications is supported by adequate and well-controlled studies in adults and pediatric patients of albuterol sulfate inhalation powder (ProAir® RespiClick). ProAir® RespiClick has been available for numerous years and has been found to be safe and effective. There is no evidence the use of the app leads to improved clinical outcomes, including safety and effectiveness. The efficacy of ProAir® Digihaler is supported by adequate and well-controlled studies in adults of ProAir® RespiClick.

Recommendation: ProAir® Digihaler be non-preferred.

Clinical Criteria:

- For the treatment of patients ≥ 4 years of age.

Board Decision: The Board unanimously approved the above recommendation.

Relafen® DS (nabumetone); **PDL category**- NSAIDs

Nabumetone, the active ingredient of Relafen® DS, is a non-steroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic, and antipyretic properties in studies. As with other NSAID agents, its mode of action is not known; however, the ability to inhibit prostaglandin synthesis may be involved in the anti-inflammatory effect. It is indicated for relief of signs and symptoms of osteoarthritis and rheumatoid arthritis. Carefully consider the potential benefits and risks of nabumetone tablets and other treatment options before deciding to use nabumetone tablets. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. The clinical studies included in the Relafen® DS prescribing information are the same as with the generically available nabumetone 500mg and 750mg tablets. Nabumetone 1000mg tablets were found to be comparable to naproxen 500mg/day

and to aspirin 3600mg/day in relieving the signs and symptoms of osteoarthritis and in relieving the signs and symptoms of rheumatoid arthritis. Nabumetone tablets, available in 500mg and 750mg, have been available for numerous years and have the same indications as Relafen® DS 1000mg tablets. Its efficacy was based on studies of nabumetone tablets, which have been available for numerous years.

Recommendation: Relafen® DS be non-preferred.

Clinical Criteria:

- Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Rinvoq® (upadacitinib, extended-release); **PDL category**- Rheumatoid Arthritis

Upadacitinib, the active ingredient of Rinvoq®, is a Janus Kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathways, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs), which modulate intracellular activity including gene expression. Upadacitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. It is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to methotrexate. Use of Rinvoq® in combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine, is not recommended. The safety and efficacy of Rinvoq® were assessed in 5 phase 3, multicenter, double-blind, randomized studies that included adults 18 years of age and older with moderately to severely active RA with the presence of at least 6 tender and 6 swollen joints and evidence of systemic inflammation based on elevation of hsCRP at baseline. Note that in the information below, upadacitinib 30mg was utilized in some studies but is not an FDA approved dose. Rinvoq® does have a box warning regarding increased risk of serious infections, malignancy, and thrombosis. In clinical trials compared with placebo, it was found to be more effective for ACR response. There some evidence in a phase 3 study to suggest that Rinvoq® may be more effective than adalimumab in RA patients when added to methotrexate; however, there is no evidence that Rinvoq® is safer or more effective than other currently available, less costly treatment options.

Recommendation: Rinvoq® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Rozlytrek® (entrectinib); **PDL category**- Cancer

Entrectinib, the active ingredient of Rozlytrek®, is a kinase inhibitor. It is an inhibitor of the tropomyosin receptor tyrosine kinases (TRK) TRKA, TRKB, and TRKC, proto-oncogene tyrosine-protein kinase ROS1 (ROS1), and anaplastic lymphoma kinase (ALK). It is indicated for the treatment of: Adult patients with

metastatic non-small cell lung cancer (NSCLC) whose tumors are *ROS1*-positive, Adult and pediatric patients 12 years of age and older with solid tumors that: Have a neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion without a known acquired resistance mutation, Are metastatic or where surgical resection is likely to result in severe morbidity, and Have either progressed following treatment or have no satisfactory alternative therapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. The safety and efficacy or Rozlytrek® were assessed in a pooled subgroup of patients with *ROS1*-positive metastatic NSCLC who received Rozlytrek® at various doses and schedules and were enrolled in 1 of 3 multicenter, single-arm, open-label clinical trials. In open-label, single-arm studies in a pooled subgroup of patients, the overall response rate was 78% for ROS1-positive non-small cell lung cancer and 57% for *NTRK* gene fusion-positive solid tumors. It is recommended that Rozlytrek® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use, and prior trials of preferred agents where appropriate.

Recommendation: Rozlytrek® be non-preferred.

Clinical Criteria:

- Rozlytrek will be considered for the treatment of: Adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive OR Adult and pediatric patients 12 years of age and older with solid tumors that: Have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation AND Are metastatic or where surgical resection is likely to result in severe morbidity, AND Have either progressed following treatment or have no satisfactory alternative therapy
- DDI: QTc interval prolongation can occur with Rozlytrek®. Avoid the concomitant use of Rozlytrek® with other products with a known potential to prolong QT/QTc interval.

Board Decision: The Board unanimously approved the above recommendation.

Rybelsus® (semaglutide); **PDL category**- Incretin Mimetics

Semaglutide, the active ingredient of Rybelsus®, is a glucagon-like peptide-1 (GLP-1) receptor agonist. It is a GLP-1 analogue with 94% sequence homology to human GLP-1 that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1. Semaglutide has a long half-life (elimination half-life of 1 week) and the main mechanism of protraction resulting in the long half-life of semaglutide is albumin binding, which results in decreased renal clearance and protection from metabolic degradation. In addition, semaglutide is stabilized against degradation by the DPP-4 enzyme. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (DM). The safety and efficacy of Rybelsus® have been studied as monotherapy and in combination with metformin, sulfonylureas, sodium-glucose co-transporter-2 (SGLT-2) inhibitors, insulins, and TZDs in patients with type 2 DM. The efficacy of Rybelsus® was compared with placebo, empagliflozin, sitagliptin, and liraglutide. In addition, Rybelsus® has been studied in patients with type 2 DM with mild and moderate renal impairment. It has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. Also, Rybelsus® is not indicated for use in patients with type 1 DM or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings. In clinical trials, Rybelsus® resulted in clinically significant reductions from baseline in HbA1c as compared with placebo. In a clinical trial compared with liraglutide SC QD, an

injectable GLP-1 receptor agonist, treatment with Rybelsus® resulted in non-inferior reductions in HbA1c as compared to liraglutide. However, in clinical trials compared with other orally active drugs, such as sitagliptin 100mg and empagliflozin 25mg, Rybelsus® 14mg resulted in a statistically significantly greater reduction in HbA1c. There is some evidence at this time from phase 3 studies to suggest that Rybelsus® is more effective than some oral antidiabetic medications, such as sitagliptin and empagliflozin. However, there is no evidence to support that Rybelsus® is safer or more effective than other currently preferred medications. It is therefore recommended that Rybelsus® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

Recommendation: Rybelsus® be non-preferred.

Clinical Criteria:

- At least two preferred drugs in this category 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.

Slynd® (drospirenone); **PDL category**- Contraceptives- Progestin Only

Drospirenone, the active ingredient of Slynd®, is for use as an oral contraceptive. Drospirenone is a spironolactone analogue with anti-mineralocorticoid activity. Slynd® is a progestin-only oral contraceptive that lowers the risk of becoming pregnant primarily by suppressing ovulation. It is indicated for the use by females of reproductive potential to prevent pregnancy. The efficacy of Slynd® was assessed in a single-arm, multicenter clinical trial conducted in the US that included females (N=953) who were ≤35 years of age with 5,547 evaluable cycles. It is not known whether the risk of VTE is increased with drospirenone alone. However, if there is a risk, it is expected to be lower than that of drospirenone in combination with ethinyl estradiol. When assessed for efficacy in 953 females, 1.8% reported pregnancy. There is no evidence at this time that Slynd® is safer or more effective than the currently preferred medications.

Recommendation: Slynd® be non-preferred.

Clinical Criteria:

- Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Tosymra® (sumatriptan); **PDL category**- Migraine- Selective Serotonin Agonists (5HT)- Tabs/Nasal

Sumatriptan, the active ingredient of Tosymra®, is a selective 5-HT1B/1D receptor agonist. It presumably exerts its therapeutic effects in the treatment of migraine headache through agonist effects at the 5-HT1B/1D receptors on intracranial blood vessels and sensory nerves of the trigeminal system, which result in cranial vessel constriction and inhibition of pro-inflammatory neuropeptide release. It is indicated for the acute treatment of migraine with or without aura in adults. Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Tosymra®, reconsider the diagnosis before Tosymra® is administered to treat any subsequent attacks. Tosymra® is not indicated for the preventive treatment of migraine and is not indicated for the treatment of cluster headache. The efficacy of Tosymra® is based on the relative bioavailability of Tosymra® nasal spray as compared to sumatriptan subcutaneous injection 4mg in healthy adults. If a patient has no response to the first migraine attack treated with Tosymra®, reconsider the diagnosis before Tosymra® is administered to treat any subsequent attacks. Tosymra® is not indicated for the preventive treatment of migraine or for the treatment of cluster headache. The efficacy of Tosymra® is based on the relative bioavailability of Tosymra® nasal spray compared to sumatriptan subcutaneous injection 4mg in healthy adults. Sumatriptan nasal spray under the brand name Imitrex® has been available for several years as 5mg and 20mg dosages, with a generic also available.

Recommendation: Tosymra® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Tovet® Foam (clobetasol propionate aerosol, foam (Emollient Formulation)); **PDL category**- Topical-Corticosteroids

Clobetasol propionate, the active ingredient of Tovet® Foam, is a synthetic corticosteroid for topical use. Clobetasol, an analog of prednisolone, has a high degree of glucocorticoid activity and a slight degree of mineralocorticoid activity. 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. It is indicated for the treatment of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses in patients 12 years and older. A randomized trial included subjects 12 years of age and older with moderate to severe atopic dermatitis who were randomized to clobetasol propionate foam, 0.05% (emulsion; N=251) or vehicle foam (N=126) twice daily for 2 weeks. It was found in clinical trials to be more effective for treatment success as compared with vehicle. Olux®-E, another clobetasol propionate foam (emollient), has the same indication as Tovet® Foam and has an available generic.

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.

Trikafta® (elexacaftor, tezacaftor, & ivacaftor kit); **PDL category**- Anti-asthmatic- CFTR Potentiator & Combinations

Trikafta® is a co-package of elexacaftor, tezacaftor, and ivacaftor fixed-dose combination tablets and ivacaftor tablets. Elexacaftor and tezacaftor bind to different sites of the cystic fibrosis transmembrane conductance regulator (CFTR) protein and have an additive effect in facilitating the cellular processing and trafficking of F508del-CFTR to increase the amount of CFTR protein delivered to the cell surface compared to either molecule alone. Ivacaftor potentiates the channel open probability (or gating) of the CFTR protein at the cell surface. It is indicated for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one *F508del* mutation. The safety and efficacy of Trikafta® were assessed in 2 phase 3, double-blind controlled trials that included patients 12 years and older with CF. . In clinical trials, Trikafta® resulted in a statistically significant treatment difference from placebo for the mean absolute change from baseline in ppFEV1 at week 4 in an interim analysis. All secondary outcomes at week 24 were statistically significantly in favor of Trikafta® when compared with placebo. In a second study with an active-comparator, treatment with Trikafta® compared to tezacaftor/ivacaftor resulted in a statistically significant improvement in ppFEV1.

Recommendation: Trikafta® be non-preferred.

Clinical Criteria:

- Trikafta will be considered for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one F508del mutation.
- Kalydeco will be considered for patients with cystic fibrosis (CF) aged 6 months and older who have one mutation in the CFTR gene that is responsive to ivacaftor potentiation based on clinical and/or in vitro assay data. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.
- Symdeko will be considered for patients with cystic fibrosis (CF) aged 6 years and older who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

Board Decision: The Board unanimously approved the above recommendation.

Turalio® (pexidartinib); **PDL category**- Cancer

Pexidartinib, the active ingredient of Turalio®, is a kinase inhibitor. Pexidartinib is a small molecule tyrosine kinase inhibitor that targets colony stimulating factor 1 receptor (CSF1R), KIT proto-oncogene receptor tyrosine kinase (KIT), and FMS-like tyrosine kinase 3 (FLT3) harboring an internal tandem duplication (ITD) mutation. It is indicated for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery. The safety and efficacy of Turalio® were assessed in a double-blind, randomized, placebo-controlled, multicenter study (ENLIVEN) that included patients with

symptomatic TGCT (also referred to as giant cell tumor of the tendon sheath [GCT-TS] or pigmented villonodular synovitis [PVNS]) for whom surgical removal of the tumor would be associated with worsening functional limitation or severe morbidity. Due to the risk of serious and potentially fatal liver injury associated with Turalio®, it has a box warning indicating liver tests should be monitored prior to the start of treatment and at specified intervals. The warning ends that due to this risk, Turalio® is available only through a restricted program called the Turalio® Risk Evaluation and Mitigation Strategy (REMS) program. In a clinical trial, a statistically significant improvement in ORR was seen in patients randomized to Turalio® as compared with placebo.

Recommendation: Turalio® Foam be non-preferred.

Clinical Criteria:

- Turalio will be considered for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery.

Board Decision: The Board unanimously approved the above recommendation.

Vyndamax® (tafamidis); **PDL category**- Neurologics- hATTR Agents

Tafamidis, the active ingredient of Vyndamax®, is a selective stabilizer of transthyretin (TTR). Tafamidis binds to TTR at the thyroxine binding sites, stabilizing the tetramer and slowing dissociation into monomers, the rate-limiting step in the amyloidogenic process. (Note that Vyndaqel® is tafamidis meglumine and available as a 20mg capsule with the same indication as Vyndamax® to be taken as 80mg daily.) It is indicated for the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization. The efficacy of Vyndamax® was demonstrated in a multicenter, randomized, double-blind, placebo-controlled study that included patients with wild type or hereditary ATTR-CM. Compared with placebo, Vyndaqel®, a 20mg capsule of tafamidis meglumine, significantly reduced all-cause mortality, cardiovascular-related hospitalization rate, and functional decline in a 30-month clinical trial. It is recommended that Vyndamax® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for its use.

Recommendation: Vyndamax® be non-preferred.

Clinical Criteria:

- PA required for appropriate diagnosis.

Board Decision: The Board unanimously approved the above recommendation.

Xembify® (immune globulin subcutaneous, human-klhw solution); **PDL category**- Immune Globulin

Xembify® contains immune globulin, human-klhw, a non-pyrogenic solution made from large pools of human plasma by a combination of cold ethanol fractionation, caprylate precipitation and filtration, and anion-exchange chromatography. Xembify® supplies a broad spectrum of opsonizing and neutralizing immunoglobulin G (IgG) antibodies against bacterial, viral, parasitic, and mycoplasma agents and their toxins. It also contains a spectrum of antibodies capable of interacting with and altering the activity of

cells of the immune system. The role of these antibodies and the mechanism of action of Xembify® are not fully understood. Adequate doses of Xembify® may restore abnormally low IgG levels to the normal range. It is indicated as a 20% immune globulin solution for SC injection indicated for treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older. This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies. A prospective, open-label, single-arm, multicenter study (Study 1) was performed to assess the pharmacokinetics and safety of Xembify® as compared to Gamunex®-C. Efficacy was based on annualized serious bacterial infection (SBI) rate during the 6 months on Xembify®. This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies. In a single-arm study, the rate of serious bacterial infections was 0.05 events per subject-year during Xembify® treatment.

Recommendation: Xembify® be non-preferred.

Clinical Criteria:

- Xembify is indicated for treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older.

Board Decision: The Board unanimously approved the above recommendation.

Xenleta® (lefamulin acetate); **PDL category**- Antibiotics, Misc

Lefamulin, the active ingredient of Xenleta®, is a semi-synthetic antibacterial agent. It is a pleuromutilin derivative that inhibits bacterial protein synthesis through interactions with the A- and P- sites of the peptidyl transferase center (PTC) in domain V of the 23s rRNA of the 50S subunit. The binding pocket of the bacterial ribosome closes around the mutilin core for an induced fit that prevents correct positioning of tRNA. It is indicated for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: *Streptococcus pneumoniae*, *Staphylococcus aureus* (methicillin-susceptible isolates), *Hemophilus influenzae*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydophila pneumoniae.* The safety and efficacy of Xenleta® were assessed in 2 multicenter, randomized, double-blind, double-dummy, non-inferiority studies that included adults (N=1289) with CABP. Study 1 compared 5 to 10 days of Xenleta® to 7 to 10 days of moxifloxacin ± linezolid. Study 2 compared 5 days of Xenleta® to 7 days of moxifloxacin. In clinical trials, it was found to be comparable to moxifloxacin. Xenleta® does have the potential to prolong the QT interval in some patients, and thus should be avoided in certain patient populations, including patients receiving other drugs that prolong the QT interval.

Recommendation: Xenleta® be non-preferred.

Clinical Criteria:

- Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

- Xenleta will be considered for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: Streptococcus pneumoniae, Staphylococcus aureus (methicillin-susceptible isolates), Hemophilus influenzae, Legionella pneumophila, Mycoplasma pneumoniae, and Chlamydophila pneumoniae.

Board Decision: The Board unanimously approved the above recommendation.

Zulresso® (brexanolone); **PDL category**- Antidepressants- Selected SSRIs

Brexanolone, the active ingredient of Zulresso®, is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator that is chemically identical to endogenous allopregnanolone. The mechanism of action of brexanolone for its indication is not fully understood, but it is thought to be related to its positive allosteric modulation of GABA-A receptors. Zulresso® is a Schedule IV controlled substance. It is indicated for the treatment of postpartum depression (PPD) in adults. The safety and efficacy of Zulresso® in the treatment of PPD were established in 2 multicenter, randomized, double-blind, placebo-controlled studies (Study 1 and 2) in women aged 18 to 45 years with PPD who met the Diagnostic and Statistical Manual of Mental Disorders criteria for a major depressive episode (DSM-IV) with onset of symptoms in the third trimester or within 4 weeks of delivery. In the studies, women received 60 hours of continuous IV infusion of Zulresso® or placebo and were followed for 4 weeks. Due to these risks, Zulresso® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Zulresso® REMS. A healthcare provider must be available on site to continuously monitor the patient, and intervene as necessary, for the duration of the Zulresso® infusion. Patients must be monitored for hypoxia and assessed for excessive sedation every 2 hours during planned, non-sleep periods. In clinical trials compared with placebo, Zulresso® titration to 90mcg/kg/hour was superior to placebo in improvement in depressive symptoms, as measured by the HAM-D total score at the end of the infusion.

Recommendation: Zulresso® be non-preferred.

Clinical Criteria:
- For the treatment of patients ≥ 18 years of age.
- Zulresso® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Zulresso® REMS.

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

MAVYRET: new dosage regimen and labeling updates
http://s2027422842.t.en25.com/e/es?s=2027422842&e=259925&elqTrackId=376c7bc788024cd5a73d955f2e3dcbdc&elq=b453859037164f5984bcdc37bfe655df&elqaid=9653&elqat=1

Sanofi Provides Update on Precautionary Voluntary Recall of Zantac OTC in U.S.
https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/sanofi-provides-update-precautionary-voluntary-recall-zantac-otc-us?utm_campaign=FDA%20MedWatch%20-%20Zantac%20150%2C%20Zantac%20150%20Cool%20Mint%2C%20Zantac%2075%20%28OTC%20Products%29%20by%20Sanofi&utm_medium=email&utm_source=Eloqua#recall-announcement

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **March 10, 2020** 5:30pm –8:30pm at the Augusta Armory.