MaineCare Services
An Office of the Department of Health and Human Services
Paul R. LePage, Governor
Ricker Hamilton, Commissioner

Department of Health and Human Services
MaineCare Services
11 State House Station
Augusta, Maine 04333-0011
Tel.: (207) 287-2674; Fax: (207) 287-2675
TTY Users: Dial 711 (Maine Relay)

**TO:** Maine Drug Utilization Review Board
**DATE:** 4/19/2018
**RE:** Maine DUR Board **Meeting** minutes from April 10, 2018

| ATTENDANCE | PRESENT | ABSENT | EXCUSED |
|---|---|---|---|
| Linda Glass, MD | | | X |
| Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR | X | | |
| Mike Antoniello, MD | | | X |
| Kathleen Polonchek, MD | X | | |
| Kenneth McCall, PharmD | X | | |
| Steve Diaz, MD | X | | |
| Erin Ackley, PharmD. | X | | |
| Corinn Martineau, PharmD. | X | | |
| **Non –Voting** | | | |
| Mike Ouellette, R.Ph., Change Healthcare | X | | |
| Jacqueline Hedlund, MD, Change Healthcare | X | | |
| Christopher Pezzullo, State Health Officer DHHS, DO | | X | |
| Jill Kingsbury, MaineCare Pharmacy Director | X | | |

**Guests of the Board:** Ed Bosshart, PharmD

## CALL TO ORDER: 5:30PM

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

## PUBLIC COMMENTS

Brian Denger: Highlighted the attributes of Exondy-51.
David Rousso from Spark Therapeutics: Highlighted the attributes of Luxterna.
Sophie Hoang from Novo Nordisk: Highlighted the attributes of Rebinyn.
Danielle Day from Novo Nordisk: Highlighted the attributes of Ozempic.
William Mullen from Indivior: Highlighted the attributes of Sublocade.
Paul Amato from Viiv: Highlighted the attributes of Juluca.
Bethany Zannrucha from Sarepta: Highlighted the attributes of Exondy-51.
Sharmi Patel from Genentech: Highlighted the attributes of Hemlibra.
Robert Arcott from Merck: Highlighted the attributes of Steglatro.

## OLD BUSINESS

## DUR MINUTES

The January DUR meeting minutes were accepted as written.

### MAINECARE UPDATE

No update at this time.

### UPDATE: CO-PRESCRIBING OF OPIOIDS (INCLUDING COUGH SYRUPS), BENZODIAZEPINES AND Z DRUGS

We did a follow-up analyst to include 2017 data. Although the numbers are still high there is a decrease in all the data points. The board found this trend data helpful and were glad to see that it was improving.

**Board Decision:** No action needed at this time

### UPDATE: CO-PRESCRIBING OF STIMULANTS, BENZODIAZEPINES AND Z DRUGS

We did a follow-up analyst to include 2017 data. After review of the numbers and different drug combinations, a suggestion was offered that a future RetroDUR examine these same combinations with the addition of naloxone.

**Board Decision:** No action needed at this time.

## NEW BUSINESS

### METHYLPHENIDATE ER/CONCERTA DISCUSSION

As was discussed at December's meeting there has been a significant price increase on these two drugs. One option is to leave Methylphenidate ER as preferred but also have Concerta (brand) as preferred. Methylphenidate CD and Methylphenidate LA could also be made preferred to open up some more options. Option two would be to make the Methylphenidate ER non-preferred and but have Concerta preferred as well as Methylphenidate CD and Methylphenidate LA.

**Board Decision:** The Board unanimously approved the above option two, moving Concerta, Methylphenidate CD and Methylphenidate LA to preferred and Methylphenidate ER to non-preferred. With the transition to happen over the summer to lessen the impact on school aged children.

### EXONDYS 51 CRITERIA UPDATE

**Exondys®51**:
•The patient must be < 14 years of age AND
• The patient must have a diagnosis of Duchenne Muscular Dystrophy with a confirmed mutation of the DMD gene that is amenable to exon 51 skipping (results of genetic testing must be submitted) AND
• 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).
•Current patient will be grandfathered but will still require re-approval after 6 months.

**Board Decision:** The Board unanimously approved the above recommendation.

## INTRODUCTION: USE OF STATINS IN ASCVD

Statin use has become widespread with the identification of the effect of cholesterol levels on risk of coronary vascular disease. Purported benefits of statins include: anti-atherogenic and plaque stabilizing properties, anti-inflammatory effects, modulation of the autonomic nervous system and anti-arrhythmic properties. Possible deleterious effects include the decrease in lipoproteins, which may help to clear bacterial endotoxins and the lowering of ubiquinone (CoEnzyme Q10).

Recommendation for statin use includes all patients with known ASCVD for secondary prevention. High dose statin therapy is recommended for most patients with LDL-C greater than 70mg/dl, although the value of high dose statins as compared with moderate dose in those over 75 years of age is unclear. It is known that statins are poorly tolerated by many and compliance is an issue. Patients should generally be prescribed the highest dose of statin tolerable, even if below guidelines.

We will use paid, non-reversed Medicaid pharmacy and medical claims date from SFY 2016 and 2017, excluding members with Part D, MaineRX, and TPL. Identify members between the ages of 40-75 with diagnoses of ASCVD and either DM, chronic kidney disease or hypercholesterolemia to see how many have been prescribed at least one statin medication for secondary prevention within the 2-year time frame. Of those prescribed at least one statin, we will look to see how many remained on a statin medication throughout the duration of the time frame we are investigating. We will stratify the data by age cohort (40-49, 50-59, 60-69, 70-75) and additionally will stratify by the intensity level of the statin prescribed to assess compliance with guidelines.

**Board Decision:** No action needed at this time.

## DATA PRESENTATION: NEW CDC GUIDELINES FOR USE OF FLUOROQUINOLONE USE, ASSESS RECENT ASAGE PATTERNS FOR SPECIFIC DIAGNOSIS (FIRST LINE, SECOND LINE TREATMENT). DIAGNOSES OF INTEREST INCLUDE SINUSITIS, PNEUMONIA/BRONCHITIS AND UTI

Fluoroquinolones are among the most prescribed antibiotics in the outpatient setting. While they have broad indications for use in respiratory, gastrointestinal, soft-tissue and systemic infections, it has been recognized that there are a variety of side-effects, some of which are severe and permanent. The incidence of muscle pain, tendonitis, tendon rupture, joint pain, neuropathy (potentially irreversible), worsening of myasthenia gravis and central nervous system effects (confusion and hallucinations) prompted an FDA advisory safety announcement that these risks generally outweigh the benefits for use in patients with acute sinusitis, acute bronchitis and uncomplicated urinary tract infections, unless no other antibiotic options exist. The FDA required drug label changes for all fluoroquinolones to reflect this safety information, as of May 2016. The black box warnings now state that fluoroquinolones should be reserved for use in patients who have no alternative treatment options for the indications of acute

exacerbation of chronic bronchitis, acute uncomplicated cystitis and acute sinusitis, and they should not be used in patients with myasthenia gravis.

We plan to examine the use of fluoroquinolones in members ages 18-65 with diagnoses of acute sinusitis, acute exacerbation of chronic bronchitis and uncomplicated UTIs, both before and after the FDA issued the safety alert and recommendations, to see if there was a measurable decrease in usage. As the FDA warning was released in May 2016, we will look at use in fiscal year 2015-2016, and compare with fiscal year 2016-2017.

We will use paid, non-reversed MaineCare pharmacy and medical claims data from SFY 2015 and 2016, excluding members with MaineRX, TPL and Part D.

These results show a rather stable use of fluoroquinolones before and after the FDA safety alert was released, however among these 3 diagnoses, use of fluoroquinolone antibiotics was relatively low (between 5 and 20% of patients). A concerning statistic is that of the 428 patients treated with a fluoroquinolone for sinusitis in 2017, only 22% (95) had received a previous antibiotic and shown a lack of improvement before the fluoroquinolone was prescribed. That was down from 30% in 2016. As there has not been an expected decrease in utilization of fluoroquinolones, education directed at the provider community is warranted. Fax Blasts containing the FDA Safety Alert and prescribing recommendations could be sent to pharmacies in the state. Directed education to the prescribers could be done in the quarterly Medicaid newsletter. Another strategy would involve identifying prescribers with high volume prescribing of fluoroquinolones and directly contact them with the FDA Safety information, although this would be a more labor-intensive strategy.

**Board Decision:** No action needed at this time. Educational information on fluoroquinolones will be sent out in the MaineCare quarterly newsletter.

## NEW DRUG REVIEW

**Admelog®** (insulin lispro); **PDL category**- Diabetic- Insulin

Insulin lispro, the active ingredient of Admelog®, is a rapid-acting human insulin analog produced by recombinant DNA technology for regulation of glucose metabolism. It lowers blood glucose by stimulating peripheral glucose uptake by skeletal muscle and fat, and by inhibiting hepatic glucose production. It is indicated to improve glycemic control in adults and pediatric patients 3 years of age and older with type 1 diabetes mellitus (DM) and in adults with type 2 DM. The safety and efficacy of Admelog® have been established based on adequate and well-controlled studies of Admelog® in adults with type 1 and type 2 DM, and based on adequate and well-controlled studies of another insulin lispro product (100U/ml) in adults and pediatric patients ≥3 years of age with type 1 DM and adults with type 2 DM.

**Recommendation:** Admelog ® be non-preferred.

**Clinical Criteria**: For the treatment of patients ≥3 years of age.

**Baxdela®** (delafloxacin meglumine); **PDL category**- Fluoroquinolones

Delafloxacin, the active ingredient of Baxdela®, is a fluoroquinolone antibacterial agent that contains meglumine salt. It works by inhibition of both bacterial topoisomerase IV and DNA gyrase (topoisomerase II) enzymes, which are needed for bacterial DNA replication, transcription, repair, and recombination. It is indicated in adults for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following: Gram-positive organisms (*Staphylococcus aureus [including MRSA and MSSA isolates]*, *Staphylococcus haemolyticus*, *Staphylococcus lugdunensis*, *Streptococcus agalactiae*, *Streptococcus anginosus* Group, *Streptococcus pyogenes*, and *Enterococcus faecalis*) and Gram-negative organisms (*Escherichia coli*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*). To reduce the development of drug-resistant bacteria and maintain the effectiveness of Baxdela® and other antibacterial drugs, Baxdela® should be used only to treat infections that are 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 Baxdela® were assessed in 2 multicenter, double-dummy, non-inferiority studies that included adults (N=1510) with acute bacterial skin and skin structure infections (ABSSSI).

**Recommendation:** Baxdela ® 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.

**benznidazole® (benznidazole); PDL category- Antiprotozoals**

Benznidazole is a nitroimidazole antimicrobial agent. It inhibits the synthesis of DNA, RNA, and proteins within the *T. cruzi* parasite. Studies suggest that benznidazole is reduced by a Type I nitroreductase (NTR) enzyme of *T. cruzi* producing a series of short-lived intermediates that may promote damage to several macromolecules including DNA. However, the exact mechanism of action is now known. It is indicated in pediatric patients 2 to 12 years of age for the treatment of Chagas disease (American trypanosomiasis) caused by *Trypanosoma cruzi*. This indication is approved under accelerated approval based on the number of treated patients who became Immunoglobulin G (IgG) antibody negative against the recombinant antigens of *T. cruzi*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The safety and efficacy of benznidazole for the treatment of Chagas disease were established in 2 adequate and well-controlled trials that included patients aged 6 to 12 years of age. It is dosed by weight and should not be administered to patients who have taken disulfiram within the last 2 weeks or with alcohol or products containing propylene glycol.

**Recommendation:** benznidazole® be preferred

**Clinical Criteria:** Clinical PA needed. For the treatment of patients 2 to 12 years of age. Benznidazole is indicated for pediatric patients 2 to 12 years of age for the treatment of Chagas disease (American trypanosomiasis) caused by *Trypanosoma cruzi*.

**Biktarvy®** (bictegravir, emtricitabine, tenofovir alafenamide fumarate); **PDL category**- Antiretrovirals

Biktarvy® is a fixed dose combination of 3 antiretroviral agents, including bictegravir (an integrase strand transfer inhibitor), emtricitabine (an HIV nucleoside analog reverse transcriptase inhibitor or HIV NRTI), and tenofovir alafenamide (an HIV NRTI). It is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA <50 copies/ml) on a stable antiretroviral regimen for at least 3 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy®. The safety and efficacy of Biktarvy® were assessed in multiple trials.

**Recommendation:** Biktarvy® be 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.

**Calquence®** (acalabrutinib); **PDL category**- Cancer

Acalabrutinib, the active ingredient of Calquence®, is an inhibitor of Bruton tyrosine kinase (BTK). Acalabrutinib and its active metabolite (ACP-5862) form a covalent bond with a cysteine residue in the BTK active site, which leads to inhibition of BTK enzymatic activity. BTK is a signaling molecule of the B cell antigen receptor (BCR) and cytokine receptor pathways. In B cells, BTK signaling results in activation of pathways needed for B-cell proliferation, trafficking, chemotaxis, and adhesion. In non-clinical studies, acalabrutinib inhibited BTK-mediated activation of downstream signaling proteins and inhibited malignant B-cell proliferation and survival. It was indicated for the treatment of adults 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 confirmatory trials. The safety and efficacy of Calquence® were assessed in an open-label phase 2 study that included subjects with MLC (N=124) who had received at least one prior treatment.

**Recommendation:** Calquence ® be non-preferred.

**Clinical Criteria**: Clinical PA required for appropriate diagnosis. DDI: Avoid concomitant use of Calquence® with strong CYP3A inhibitors and strong CYP3A inducers.

**Yescarta®** (axicabtagene ciloleucel); **PDL category**- Cancer

Yescarta® is a CD19-directed genetically modified autologous T cell immunotherapy. To prepare, a patient's own T cells are harvested and genetically modified ex vivo by retroviral transduction to express a chimeric antigen receptor (CAR) comprising a murine anti-CD19 single chain variable fragment linked to CD28 and CD3-zeta co-stimulatory domains. The anti-CD19 CAR T cells are expanded and infused back into the patient, where they can recognize and eliminate CD19-expressing target cells. Yescarta® binds to CD19-expressing cancer cells and normal B cells. The sequence of events leads to killing of CD19-expressing cells. It is indicated as a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adults with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma,

high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. Yescarta® is not indicated for the treatment of patients with primary central nervous system lymphoma. The efficacy of Yescarta® was assessed in a single-arm, open-label, multicenter study that included adult patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma. Of the 111 patients who underwent leukapheresis, 101 received Yescarta®. Efficacy was established on the basis of complete remission rate and duration of response, per an independent review committee. The median time to response was 0.9 months (range 0.8 to 6.2 months). Response durations were longer in patients who achieved complete response as compared to patients with a best response of partial remission.

**Recommendation:** Yescarta ® be non-preferred.

**Clinical Criteria**: Clinical PA required for appropriate diagnosis. For treatment of adults with relapse or refractory large B-cell lymphoma after 2 or more lines of chemotherapy (as Kymriah does for ALL in children).

**Cinvanti®** (aprepitant); **PDL category**- Antiemetic- 5-HT3 Receptor Antagonists/Substance P Neurokinin

Aprepitant, the active ingredient of Cinvanti®, is a substance P/neurokinin 1 (NK1) receptor antagonist, an anti-emetic agent. In animals, it has been shown to inhibit emesis induced by cytotoxic chemotherapeutic agents, such as cisplatin, via central actions. Animal and human studies have demonstrated that aprepitant augments the anti-emetic activity of the 5-HT3 receptor antagonist ondansetron and the corticosteroid dexamethasone and inhibits both the acute and delayed phases of cisplatin-induced emesis. It was indicated in combination with other anti-emetic agents, is indicated in adults for the prevention of: acute and delayed nausea and vomiting with initial and repeat course of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin AND nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). Cinvanti® has not been studied for the treatment of established nausea and vomiting. The safety and efficacy of Cinvanti® were established based on adequate and well-controlled adult studies of a single-dose of IV fosaprepitant, a pro-drug of aprepitant, and a 3-day regimen of oral aprepitant in chemotherapy-induced nausea and vomiting associated with HEC and MEC, respectively.

**Recommendation:** Cinvanti ® be non-preferred.

**Clinical Criteria**: Clinical PA required for appropriate diagnosis. Preferred drugs and step therapy 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.

**Cotempla®XR (methylphenidate extended-release); PDL category-** Stimulants- Methylphenidate, Long Acting

Methylphenidate, the active ingredient of Cotempla® XR, is a central nervous system (CNS) stimulant. While the exact mode of therapeutic action in ADHD is not known, it is thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and thus increase the release of these monoamines into the extra-neuronal space. Cotempla® XR is a Schedule II controlled substance. As such, it has a box warning regarding a high potential for abuse and dependence. It is recommended to assess the risk of abuse prior to prescribing and to monitor for signs of abuse and dependence during

treatment. It is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age. The safety and efficacy of Cotempla® XR were assessed in a small (N=87) laboratory classroom study that included pediatric patients aged 6-12 years with ADHD.

**Recommendation:** Cotempla® XR 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.

**Duzallo®** (lesinurad/allopurinol); **PDL category**- Gout

Duzallo® is a combination tablet containing two medications with complementary mechanisms of actions that includes lesinurad (a uric acid reabsorption inhibitor) and allopurinol (a xanthine oxidase inhibitor). Both active ingredients work to lower serum uric acid levels by increasing excretion and inhibiting production of uric acid, respectively. It is indicated for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with a medically appropriate daily dose of allopurinol alone. Duzallo® is not recommended for the treatment of asymptomatic hyperuricemia. There were no phase 3 studies with Duzallo®. Bioequivalence of Duzallo® to co-administered lesinurad and allopurinol was demonstrated, and the efficacy of the combination of allopurinol and lesinurad has been demonstrated in two phase 3, randomized, double-blind, placebo-controlled studies. Results of these studies demonstrated that lesinurad 200mg plus allopurinol was superior to allopurinol alone for lowering serum uric acid to less than 6mg/dl at month 6

**Recommendation:** Duzallo ® 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.

**Fasenra®** (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 surfaced 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 for 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. There are no contraindications with use or drug interactions found. It was found in clinical trials to be significantly 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® 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.

**Fibryga®** (fibrinogen concentrate(human)); **PDL category**- Hemostatic

Fibryga® is a human plasma-derived, sterile, purified, virus-inactivated and nanofiltered fibrinogen concentrate. All units of human plasma used in the manufacture of Fibryga® are provided by FDA-approved blood establishments, and are tested by FDA-licensed serological tests for hepatitis B surface antigen (HBsAg), antibodies to hepatitis C virus, and HIV-1/2. It is also screened for other viruses, and only plasma that passed virus screening is used for production. The manufacturing process includes a solvent/detergent step for virus inactivation and a nanofiltration step for virus removal. Fibrinogen (Factor I) is a soluble plasma protein that, during the coagulation process, is converted to fibrin, one of the main components of the blood clot. Use in patients with congenital fibrinogen deficiency supplements the missing coagulation factor or increases low plasma fibrinogen levels. Normal plasma fibrinogen level is in the range of 200-45mg/dl. It is indicated for the treatment of acute bleeding episodes in adults and adolescents with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. Fibryga® is not indicated for dysfibrinogenemia. An interim analysis of an ongoing, prospective, open-label, uncontrolled, multicenter study was conducted in 13 patients with congenital fibrinogen deficiency. The patients ranged in age from 13 to 53 years, including 2 adolescents and 11 adults. The data discussed describes 22 minor bleeding events, with minor bleeding defined as mild joint bleeding or superficial muscle, soft tissue, and oral bleeding. Fifteen bleeding events (68%) were spontaneous and 7 bleeding events (32%) were traumatic.

**Recommendation:** Fibryga ® be non-preferred.

**Clinical Criteria**: **Fibryga and Riastap** are indicated for the treatment of acute bleeding episodes in adults and adolescents with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.
**Fibryga**® is not indicated for dysfibrinogenemia.

**Hemlibra®** (emicizumab-kxwh); **PDL category**- Antihemophilic Agents

Emicizumab-kxwh, the active ingredient of Hemlibra®, is a human monoclonal modified immunoglobulin G4 (IgG4) antibody with a bio-specific antibody structure binding factor IXa and factor X. Emicizumab-kxwh has no structural relationship or sequence homology to FVIII and, as such, does not induce or enhance the development of direct inhibitors to FVIII. Hemlibra® bridges activated factor IX and factor X to restore the function of missing activated factor VIII that is needed for effective hemostasis. It is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors. The safety and efficacy of Hemlibra® for routine prophylaxis in patients with Hemophilia A with FVIII inhibitors were assessed in 2 clinical trials, including an adult/adolescent study (HAVEN 1) and a pediatric study (HAVEN 2).

**Recommendation:** Hemlibra ® be preferred with clinical PA.

**Clinical Criteria**: Clinical PA is required to establish diagnosis and medical necessity.

**Juluca®** (dolutegravir sodium and rilpivirine); **PDL category**- Antiretrovirals

Juluca® is a fixed-dose combination tablet containing human immunodeficiency virus type 1 (HIV-1) antiretroviral agents, including dolutegravir (an integrase strand transfer inhibitor or INSTI) and rilpivirine (a non-nucleoside reverse transcriptase inhibitor or NNRTI). Dolutegravir inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral DNA integration, which is needed for the HIV replication cycle. Rilpivirine inhibits HIV-1 replication by non-competitive inhibition of HIV-1 reverse transcriptase. It is indicated as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA <50 copies/ml) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Juluca®. The safety and efficacy of Juluca® were assessed in 2 open-label controlled trials (SWORD-1 and SWORD-2) that included virologically suppressed patients switching from their current antiretroviral regimen to dolutegravir plus rilpivirine-taken as two separate drugs.

**Recommendation:** Juluca ® 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.

**Ozempic®** (semaglutide); **PDL category**- Incretin Mimetic

Semaglutide, the active ingredient of Ozempic®, is a human glucagon-like peptide 1 (GLP-1) receptor agonist or GLP-1 analog. It is a GLP-1 analog with 94% sequence homology to human GLP-1. It acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor. GLP-1 is a physiological hormone that has multiple actions on glucose. It stimulates insulin secretion and lowers glucagon secretion to reduce blood glucose. It has an elimination half-life of about 1 week, thus it will be present in the circulation for about 5 weeks after the last dose. It is indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Ozempic® is not recommended as a first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of rodent C-cell tumor findings to humans. It has not been studied in patients with a history of pancreatitis; thus, consider other antidiabetic therapies in patients with a history of pancreatitis. In addition, Ozempic® is not a substitute for insulin. It is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings. Numerous studies were performed to assess the safety and efficacy of Ozempic®, as compared with placebo, sitagliptin, exenatide ER, and insulin glargine. In patients with type 2 DM, Ozempic® produced clinically relevant reductions from baseline in HbA1c as compared with placebo.

**Recommendation:** Ozempic® be non-preferred. Add Bydureuon Bcise to 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.

**Prevymis®** (letermovir); **PDL category**- Cyto megalovirus Agents

Letermovir, the active ingredient of Prevymis®, is an antiviral agent. It is an inhibitor of the cytomegalovirus DNA terminase complex which is required for viral DNA processing and packaging. It is indicated for prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT). The safety and efficacy of Prevymis® were assessed in a multicenter, randomized, double-blind, phase 3 study that included adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT). Subjects were randomized to receive either Prevymis® or placebo, with the study drug administered as either PO or IV. All received CMV DNA monitoring weekly until post-transplant week 14 and then bi-weekly until post-transplant week 24, with initiation of standard-of-care CMV pre-emptive therapy if CMV viremia was considered clinically significant. The efficacy population consisted of 325 patients who received Prevymis® and 170 who received placebo. The primary endpoint was the incidence of clinically significant CMV infection through week 24 post-transplant. There is no evidence at this time to support that Prevymis® is safer or more effective than the currently available, more cost effective, medications.

**Recommendation:** Prevymis ® be non-preferred.

**Clinical Criteria**: **Prevymis**: Documentation that member is high-risk for CMV reactivation as defined by transplant guidelines or that there has been significant myelosuppression by one of the preferred agents.

**Qtern®** (dapagliflozin and saxagliptin); **PDL category**- Diabetic- DPP-4 Enzyme Inhibitor-Combo

Qtern® is a combination tablet containing dapagliflozin (an active inhibitor of sodium-glucose cotransporter 2, or SGLT-2) and saxagliptin (an active inhibitor of the dipeptidyl-peptidase-4, or DPP-4 enzyme). By inhibiting SGLT-2, dapagliflozin reduces reabsorption of filtered glucose and lowers the renal threshold for glucose, thus increasing urinary glucose excretion. Saxagliptin works to slow the inactivation of the incretin hormones, thus increasing their bloodstream concentrations and reducing fasting and postprandial glucose concentrations in a glucose-dependent manner. It is indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) who have inadequate control with dapagliflozin or who are already treated with dapagliflozin and saxagliptin. It is not indicated for the treatment of type 1 DM or diabetic ketoacidosis. Qtern® should only be used in patients who tolerate 10mg dapagliflozin. Specific studies weren't performed with Qtern®; however, an add-on therapy with saxagliptin study in patients on dapagliflozin plus metformin was included in the prescribing information of Qtern®. A randomized, double-blind, placebo-controlled study was performed to assess the safety and efficacy of saxagliptin added to dapagliflozin and metformin as compared to placebo in adults with a baseline HbA1c between ≥7% to ≤10.5%.

**Recommendation:** Qtern ® 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.

**Rebinyn®** (coagulation factor IX (recombinant). Glyco-pegylated); **PDL category**- Antihemophilic Agents

Rebinyn® is a purified recombinant human Factor IX (rFIX) with a polyethylene-glycol (PEG) conjugated to the protein. This PEG molecule slows down its removal from circulation. This product goes through a purification process. Hemophilia B patients are deficient in coagulation Factor IX, which is needed for effective hemostasis. Treatment with Rebinyn® temporarily replaces the missing coagulation Factor IX. It is indicated a recombinant DNA-derived coagulation Factor IX concentrate indicated for use in adults and children with hemophilia B for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding

Rebinyn® is not indicated for routine prophylaxis in the treatment of patients with hemophilia B. Rebinyn® is not indicated for immune tolerance induction in patients with hemophilia B. There were 4 multicenter, non-controlled studies performed to assess the safety and efficacy of Rebinyn® in routine treatment, on-demand treatment and perioperative management in previously treated male patients with hemophilia B. The efficacy evaluation included 105 subjects, with 62 adults, 18 adolescents (13 to 17 years), and 25 children (1 to 12 years).

- The adult/adolescent trial included 74 adolescents and adults previously treated. There were 2 routine treatment arms, with single-blind randomization for 52 weeks and an open-label on-demand treatment arm for 28 weeks.

- The surgery trial included 13 previously treated adolescent and adult patients who received one infusion of Rebinyn® the day of the surgery and post-operatively received infusions at the investigators discretion for up to 3 weeks.

- The adult/adolescent extension trial included 71 subjects from the adult/adolescent trial and surgery trial who continued routine treatment or on-demand treatment with Rebinyn® in an open-label extension trial.

- The pediatric trial included 25 pediatric previously treated patients where subjects received routine Rebinyn® treatment once weekly for 52 weeks.

There was a total of 597 bleeding episodes reported in 79 out of 105 patients in the clinical program in previously treated patients. An overall assessment of efficacy was performed by the subjects (for home treatment) or the study site investigator (for treatment under medical supervision), using a 4-point scale of excellent, good, moderate, or poor. The overall success rate, defined as excellent or good, for treatment of bleeding episodes was 93.2%.

**Recommendation:** Rebinyn ® be non-preferred.

**Clinical Criteria**: **Rebinyn®** is not indicated for routine prophylaxis in the treatment of patients with hemophilia B or for immune tolerance induction in patients with hemophilia B.

**Renflexis®** (infliximab-abda); **PDL category**- Rheumatoid Arthritis

Infliximab-abda, the active ingredient of Renflexis®, is a biosimilar to Remicade® (infliximab). It is a chimeric IgG1k monoclonal antibody specific for human tumor necrosis factor-alpha (TNF-alpha). Infliximab products

neutralize the biological activity of TNF-alpha by binding with high affinity to TNF alpha and inhibit the binding of TNF alpha with its receptors. Renflexis is indicated for the following:

- Crohn's Disease (CD): To reduce signs/symptoms and induce/maintain clinical remission in adults with moderately to severely active CD who have had an inadequate response to conventional therapy AND to reduce the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adults with fistulizing CD
- Pediatrics Crohn's Disease: To reduce signs/symptoms and induce/maintain clinical remission in pediatric patients ≥6 years of age with moderately to severely active CD who have had an inadequate response to conventional therapy
- Ulcerative Colitis (UC): To reduce signs/symptoms, induce/maintain clinical remission and mucosal healing, and eliminate corticosteroid use in adults with moderately to severely active UC who had an inadequate response to conventional therapy
- Rheumatoid Arthritis (RA): In combination with methotrexate to reduce signs/symptoms, inhibit the progression of structural damage, and improve physical function with moderately to severely active RA
- Ankylosing Spondylitis (AS): To reduce signs/symptoms in patients with active AS
- Psoriatic Arthritis (PA): To reduce signs/symptoms of active arthritis, inhibit progression of structural damage, and improve physical function
- Plaque Psoriasis (PP): Chronic severe PP for adults who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. Should only be administered to those who will be closely monitored and have regular follow-up visits with physician.

Renflexis® has a box warning regarding the increased risk of serious infections and malignancy with use. Serious infections may lead to hospitalization or death. Treatment should be discontinued if a serious infection or sepsis develops. The risks and benefits of treatment with Renflexis® should be carefully considered prior to starting therapy in patients with chronic or recurrent infection. In addition, the box warning also indicates lymphoma and other malignancies, some fatal, have been reported in children and adolescents treated with TNF blockers, including infliximab products. Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL) have been reported in patients treated with TNF blockers, including infliximab products. Renflexis® is the second biosimilar to Remicade® (infliximab) approved by the FDA. Per the FDA site, "a biosimilar product is a biological product that is approved based on showing that it is highly similar to an already-approved biological product, known as the reference product. The biosimilar must also show that it has no clinically meaningful differences in terms of safety and effectiveness from the reference product. Only minor differences in clinically inactive components are allowable in biosimilar products."[2] In addition, "a biosimilar product can only be approved by the FDA if it has the same mechanism(s) of action (but only to the extent that the mechanism(s) of action are known for the reference product), route(s) of administration, dosage form(s) and strength(s) as the reference product, and only for the indication(s) and condition(s) of use that have been approved for the reference product."[2]

**Recommendation:** Renflexis ® 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.

**Riastap®** (fibrinogen concentrate); **PDL category**- Hemostatic

Riastap® is lyophilized fibrinogen (coagulation factor 1) concentrate powder manufactured from pooled human plasma. All plasma is tested using serological assays for hepatitis B surface antigen and antibodies to HIV and hepatitis C virus, among others. The manufacturing process has been demonstrated to reduce the risk of virus transmission in several steps. Administration of Riastap® to patients with congenital fibrinogen deficiency replaces missing or low levels of coagulation factor. Normal levels are in the range of 200 to 450mg/dl. It is indicated as a human blood coagulation factor indicated for the treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. The efficacy of Riastap® was based on maximum clot firmness, a measure of clot structural integrity that reflects the underlying effectiveness of the fibrinogen present to form a fibrin clot. A study was performed and maximum clot firmness (MCF) in subjects with afibrinogenemia was assessed. MCF was determined by thromboelastometry (ROTEM) testing and was used to demonstrate functional activity of replacement fibrinogen when a fixed dose of Riastap® was given.

**Recommendation:** Riastap® be non-preferred.

**Clinical Criteria**: **Fibryga and Riastap** are indicated for the treatment of acute bleeding episodes in adults and adolescents with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

**Solosec®** (secnidazole); **PDL category**- Antibiotics, Misc.

Secnidazole, the active ingredient of Solosec®, is a nitroimidazole antimicrobial drug. It is a 5-nitroimidazole that enters the bacterial cell as an inactive prodrug where the nitro group is reduced by bacterial enzymes to radical anions. It is thought that these radical anions interfere with bacterial DNA synthesis of susceptible isolates. It is indicated for the treatment of bacterial vaginosis in adult women. To reduce the development of drug-resistant bacteria and maintain the effectiveness of Solosec® and other antibacterial drugs, Solosec® should be used only to treat or prevent infections that are 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 Solosec® were assessed in 2 randomized placebo controlled trials with similar designs that included non-pregnant females with bacterial vaginosis.

**Recommendation:** Solosec ® 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.

**Steglatro®** (ertugliflozin); **PDL category**- SGLT2 Inhibitors

Ertugliflozin L-pyroglutamic acid, the active ingredient of Steglatro®, is a sodium glucose co-transporter 2 (SGLT2) inhibitor, the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. By inhibiting SGLT2, ertugliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, thus increases urinary glucose excretion. It is indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (DM). It is not recommended in patients with type 1 DM or for the treatment of diabetic ketoacidosis. The safety and

efficacy of Steglatro® have been assessed in 7 multicenter, randomized, double-blind, placebo- or active-controlled studies that included adults with type 2 DM.

**Recommendation:** Steglatro® 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.

**Sublocade®** (buprenorphine extended- release); **PDL category**- Opioid Dependence Treatments

Buprenorphine free base, the active ingredient of Sublocade®, is a mu-opioid receptor partial agonist and a kappa-opioid receptor antagonist. Sublocade® is a Schedule III substance under the Controlled Substances Act. It can be abused in a manner like other opioids. It is subject to addiction, abuse, and misuse. Monitor all patients for progression of opioid use disorder and addictive behaviors. It is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days. Sublocade® should be used as part of a complete treatment plan that includes counseling and psychosocial support. The safety and efficacy of Sublocade® for the treatment of opioid use disorder were assessed in a randomized, multicenter, double-blind, placebo-controlled study that included treatment-seeking patients who met the DSM-5 criteria for moderate or severe opioid use disorder. Sublocade® is an abdominal subcutaneous injection indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days. It should be used as part of a complete treatment plan that includes counseling and psychosocial support. If the depot must be removed, it can be surgically excised under local anesthesia within 14 days of injection. It is a Schedule III controlled substance and thus has a warning of addiction, abuse, and misuse. Due to the risk of serious harm or death with IV use, it has a box warning indicating that it is only available through a restricted program called the Sublocade® REMS program. In a phase 3 clinical study, it was found to be superior to placebo for achieving treatment success and for having a higher percentage of urine samples negative for illicit drugs. Sublocade® is not appropriate for use in opioid naïve patients.

**Recommendation:** Sublocade® 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.

**Vyzulta®** (latanoprostene bunod); **PDL category**- Ophthalmics - Prostaglandins

Latanoprostene bunod, the active ingredient of Vyzulta®, is a prostaglandin analog. It is thought to lower intraocular pressure by increasing outflow of aqueous humor through both the trabecular meshwork and uveoscleral routes. Reduction of intraocular pressure reduces the risk of glaucomatous visual field loss. Reduction of intraocular pressure starts about 1 to 3 hours after the first administration. It is indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. There is some evidence at this time that may suggest that Vyzulta® is more effective than timolol and latanoprost

in a clinical trial; however, there is no evidence that it is safer or more effective than other available, more cost-effective medications available.

**Recommendation:** Vyzulta® 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 all of the above recommendation.

## FDA SAFETY ALERTS

FDA Drug Safety Communication: FDA warns about serious liver injury with Ocaliva (obeticholic acid) for rare chronic liver disease
https://www.fda.gov/Drugs/DrugSafety/ucm576656.htm

**Board Decision:** No formal action required

## ADJOURNMENT: 8:30PM

The next meeting will be held on **June 12, 2018** 5:30pm –8:30pm at the Augusta Armory.