MaineCare Services
An Office of the Department of Health and Human Services
Paul R. LePage, Governor Mary C. Mayhew, Commissioner

Department of Health and Human Services
MaineCare Services
Pharmacy Unit
11 State House Station
Augusta, Maine 04333-0011
Toll Free (866) 796-2463; Fax: (207) 287-8601
TTY Users: Dial 711 (Maine Relay)

TO: Maine Drug Utilization Review Board
DATE: 1/25/2018
RE: Maine DUR Board **Meeting** minutes from January 16, 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:

CALL TO ORDER: 5:30PM

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

PUBLIC COMMENTS

Alice Senko from Celgene: Highlighted the attributed of Idhifa.
Alexander Patschenko from Pfizer presented.

OLD BUSINESS

DUR MINUTES

The October DUR meeting minutes were accepted as written.

MAINECARE UPDATE

No update at this time.

NEW BUSINESS

INTRODUCTION: 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, PNEUMONIE/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 identify members on a fluoroquinolone with a diagnosis of acute sinusitis, acute bronchitis exacerbation of chronic bronchitis or uncomplicated UTI. We will compare usage as a percentage of members who received a fluoroquinolone in the total member population for each year and examine the diagnosis associated with the members who received fluoroquinolones. Because a fluoroquinolone may be ordered appropriately in members who failed prior antibiotic therapy, we will look to see if other classes of antibiotics had been prescribed for the same diagnosis, prior to the prescribing of the fluoroquinolone, within the fiscal year. We expect to see less usage of fluoroquinolones after the FDA safety alert was published.

Board Decision: No action needed at this time

DATA PRESENTATION: COMPLIANCE WITH GLP-1 AGONISTS IN TYPE II DIABETES MELLITUS 2018 MEETING SCHEDULE

GLP-1 (glucagon-like peptide 1 receptor) agonists are incretin mimetics which have several benefits for diabetes management. They suppress post-prandial glucagon release, delay stomach emptying, and increase insulin sensitivity. Significantly lower rates of hypoglycemia accompany GLP-1 therapy than many alternative hypoglycemics including insulin and sulfonylureas. This class also has the side effect of modest weight reduction and reduction of systolic blood pressure. Although they improve glycemic control, there are few long-term studies of GLP-1 agonists to assess clinically important health outcomes (cardiovascular events, mortality), durability of weight loss, or safety. Many questions remain unanswered regarding clinical use in type 2 diabetes, including long-term benefits and risks and their role in combination with other diabetes medications.

Although the standard has been to add insulin or sulfonylurea as the second step for patients who fail initial therapy with lifestyle intervention and metformin, the addition of a GLP-1 receptor agonist is an alternative, although expensive, option listed in both the ADA and ACE guidelines, especially if avoidance of hypoglycemia is a high priority. GLP-1 receptor agonists are more often prescribed in combination with metformin (and/or another oral agent) for patients who fail initial therapy with one or two oral agents, particularly when weight loss or avoidance of hypoglycemia is a primary consideration, the A1C level is close to target (within 1 to 1.5 percentage points), and cost or injection therapy are not major barriers. Because the GLP-1 drugs are all injectable, compliance is an issue that must be addressed. In addition, 5% of patients in clinical trials discontinued the drugs due to the GI side effects of nausea, vomiting and diarrhea. In clinical practice, it is estimated that 5-10% of patients discontinue the medications due to GI intolerance.

609 unique members were identified as users of a GLP-1 agonist. Of those, 103 were tried on more than one GLP-1 agonist or different strengths of the same GLP-1 agonist, so there were a total of 712 member/medication combinations. 645 (77%) had an MPR > 0.8 which is considered adherent. 207 (24%) had an MPR < 0.8, which could indicate that approximately 24% of the time members are not adherent to their GLP-1 agonist as prescribed. It is interesting to note that the majority of patients 85% who changed to a different strength or GLP-1 medication, had an MPR > 0.8 for at least one of the GLP-1 agonists.

555 members had at least 1 other anti-diabetic prescription filled concurrently with their GLP-1 agonist. 397 members had at least 2 other anti-diabetic medications, and 54 patients were identified as being on a GLP-1 agonist only. The table below illustrates the breakdown of other diabetic medications being taken along with a GLP-1 agonist.

Board Decision: No action needed at this time

RETRO-DUR -PRESENT 2018 CALENDER

The general work plan is to bring information about the next planned initiative to the DUR Committee for discussion/modification. The data will then be analyzed and presented roughly 60-90 days later. The calendar below illustrates this. If further data analysis is requested, this can be presented at a later meeting.

- **March 13, 2018:**
  - Data presentation: *Use of Fluoroquinolones*
  - Introduce: *Statin Use in Congestive Heart Failure*
- **June 12, 2018:**
  - Data presentation: *Statin Use in Congestive Heart Failure*
  - Introduce: *Naloxone Intolerance*
- **September 11, 2018**
  - Data presentation: *Naloxone Intolerance*
  - Introduce: *Chronic Triptan Use*
- **October 9, 2018:**
  - Introduce: *Topics for 2019 RetroDUR Initiatives*
- **December 11, 2018:**
  - Date presentation: 2019 RetroDUR Calendar
  - Data presentation: *Chronic Triptan Use*
  - Introduce: *Vivitrol Adherence*
- **Meeting #1, 2019:**
  - Introduce: *1st RetroDUR initiative for 2019*
  - Data presentation: *Vivitrol Adherence*

Board Decision: No formal action required

2018 PDL UPDATE

Update from the pending voting from the October meeting.

Butrans- will remain Preferred on the PDL
Epi Pen- Will remain Preferred on the PDL

NEW DRUG REVIEW

Aliqopa® (copanlisib); **PDL category**- Cancer

Copanlisib, the active ingredient of Aliqopa®, is a kinase inhibitor. It is an inhibitor of phosphatidylinositol-3-kinase (PI3K) with inhibitor activity mainly against PI3K-α isoforms expressed in malignant B cells. Copanlisib has been shown to induce tumor cell death by apoptosis and inhibition of proliferation of primary malignant B cell lines. It inhibits several key cell-signaling pathways, including B-cell receptor (BCR) signaling, CXCR12 mediated chemotaxis of malignant B cells, and NFkB signaling in lymphoma cell lines. It is indicated for the treatment of adult patients with relapsed follicular lymphoma (FL) who have received at least 2 prior systemic therapies. The recommended dose is to infuse 60mg administered as a 1-hour IV infusion on days 1, 8, and 15 of a 28-day treatment cycle on an intermittent schedule (3 weeks on and 1 week off). Continue treatment until disease progression or unacceptable toxicity. Refer to the prescribing information for information regarding dose modifications for toxicities, including infections, hyperglycemia, hypertension, non-infectious pneumonitis, neutropenia, severe cutaneous reactions, thrombocytopenia, and other severe and non-life-threatening toxicities. Accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Recommendation: Aliqopa ® be non-preferred.

Clinical Criteria: Clinical PA required for appropriate diagnosis

Besponsa® (inotuzumab ozogamicin); **PDL category**- Cancer

Inotuzumab ozogamicin is a CD22-directed antibody-drug conjugate (ADC) consisting of 3 components: the recombinant humanized immunoglobulin class G subtype 4 (IgG4) kappa antibody inotuzumab, specific for human CD22; N-acetyl-gamma-calicheamicin that causes double-stranded DNA breaks; and an acid-cleavable linker composed of the condensation product known as dimethylhydrazide that covalently attaches N-acetyl-gamma-calicheamicin to inotuzumab.

Inotuzumab recognizes human CD22. Data suggests that the anti-cancer activity of inotuzumab ozogamicin is due to the binding of the ADC to CD22-expressing tumor cells, followed by internalization of the ADC-CD22 complex, and the intracellular release of N-acetyl-gamma-calicheamicin dimethylhydrazide via hydrolytic cleavage of the linker. Activation of N-acetyl-gamma-calicheamicin dimethylhydrazide induces double-strand DNA breaks, subsequently inducing cell cycle arrest and apoptotic cell death. It is indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). The safety and efficacy of Besponsa® were assessed in a randomized, open-label, multicenter study (INO-VATE ALL) that included adults ≥18 years with relapsed or refractory ALL (N=326) wo were randomized to Besponsa® or Investigator's choice of chemotherapy.

Recommendation: Besponsa ® be non-preferred.

Clinical Criteria: Approvals will require previous trial of corticosteroids, antimalarials, NSAIDS and immunosuppressives. DDI: Concomitant use of Besponsa® with drugs known to prolong the QT interval or induce Torsades de Pointes may increase the risk of a clinically significant QTc interval prolongation.

Idihfa® (enasidenib); PDL category- Cancer

Enasidenib, the active ingredient of Idhifa®, is an inhibitor of isocitrate dehydrogenase-2 (IDH2) enzyme. It is a small molecule inhibitor of the IDH2 enzyme that targets the mutant IDH2 variants at about a 40-fold lower concentration than the wild-type enzyme in vitro. Inhibition of the mutant IDH2 enzymes by enasidenib led to decreased 2-hydroxyglutarate (2-HG) levels and induced myeloid differentiation in vitro and in vivo in mouse models of IDH2 mutated acute myeloid leukemia (AML). In blood samples from patients with AML with mutated IDH2, enasidenib decreased 2-HG levels, reduced blast counts, and increased percentages of mature myeloid cells. It is indicated for the treatment of adult patients with relapsed or refractory AML with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test. The safety and efficacy of Idhifa® were assessed in an open-label, single-arm, multicenter, two-cohort study that included adults with relapsed or refractory AML and an IDH2 mutation.

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

Clinical Criteria: Clinical PA required for appropriate diagnosis.

Kymriah® (tisagenlecleucel); **PDL category**- Cancer

Tisagenlecleucel, the active ingredient of Kymriah®, is a CD19-directed genetically modified autologous T cell immunotherapy comprised of autologous T cells that are genetically modified using a lentiviral vector to encode an anti-CD19 chimeric antigen receptor (CAR). It involves reprogramming a patient's own T cells with a transgene encoding a CAR to identify and eliminate CD19 expressing malignant and normal cells. The CAR is comprised of a murine single-chain antibody fragment which recognizes CD19 and is fused to intracellular signaling domains from 4-1BB (CD137) and CD3 zeta. The CD3 zeta component is critical for initiating T-cell activation and antitumor activity, while 4-1BB enhances the expansion and persistence of Kymirah®. With binding to CD19 expressing cells, the CAR transmits a signal to promote T-cell expansion, activation, target cell elimination, and persistence of the Kymriah® cells. It is for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

Recommendation: Kymriah ® be non-preferred.

Clinical Criteria: Clinical PA required for appropriate diagnosis. For the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

Mylotarg® (gemtuzumab ozogamicin); **PDL category**- Cancer

Gemtuzumab ozogamicin, the active ingredient of Mylotarg®, is an antibody-drug conjugate (ADC) composed of the CD33-directed monoclonal antibody (hP67.6; recombinant humanized immunoglobulin (Ig) G4 kappa) that is covalently linked to the cytotoxic agent N-acetyl gamma calicheamicin. It is a CD33-directed ADC, and the antibody portion (hP67.6) recognizes human CD33 antigen. Data suggests that the anticancer activity of gemtuzumab is due to the binding of the ADC to CD33-expressing tumor cells, followed by internalization of the ACD-CD33 complex and the intracellular release of N-acetyl gamma calicheamicin dimethyl hydrazide via hydrolytic cleavage of the linker. Activation of N-acetyl gamma calicheamicin dimethyl hydrazide induces double-strand DNA breaks, subsequently inducing cell cycle arrest and apoptotic cell death. It is indicated for the treatment of newly-diagnosed CD33-positive acute myeloid leukemia (AML) in adults AND for the treatment of relapsed or refractory CD33-positive AML in adults and in pediatric patients ≥2 years.

Recommendation: Mylotarg ® be non-preferred.

Clinical Criteria: Clinical PA required for appropriate diagnosis

Nerlynx® (neratinib); **PDL category**- Cancer

Neratinib, the active ingredient of Nerlynx®, is a protein kinase inhibitor that irreversibly binds to the Epidermal Growth Factor Receptor (EGFR), Human Epidermal Growth Factor Receptor 2 (HER2), and HER4. It is indicated for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab based therapy. Antidiarrheal prophylaxis is recommended during the first 2 cycles of treatment and should be started with the first dose of Nerlynx®. It is recommended to take loperamide 4mg 3 times daily weeks 1-2, 4mg twice daily weeks 3-8, and 4mg as needed (max 16mg per day) on weeks 9-52. Further antidiarrheal medications may be needed to manage diarrhea in patients with loperamide-refractory diarrhea. Dose interruptions and dose reductions of Nerlynx® may be needed. Avoid the concomitant use of proton pump inhibitors or H2-receptor antagonists with Nerlynx®. The safety and efficacy of Nerlynx® were assessed in a multicenter, randomized, double-blind, placebo-controlled study (ExteNET study). Women (N=2840) with early-stage HER2-positive breast cancer within 2 years of completing treatment with adjuvant trastuzumab were randomized to Nerlynx® or placebo.

The main efficacy outcome was invasive disease-free survival (iDFS), defined as the time between the date of randomization to the first occurrence of invasive recurrence, distant recurrence, or death from any cause, with 2 years and 28 days of follow-up. Most patients (81%) were enrolled within 1 year of completion of trastuzumab treatment. The median time from the last adjuvant trastuzumab treatment to randomization was 4.4 months in the Nerlynx® arm vs 4.6 months in the placebo arm. The median duration of treatment was 11.6 months with Nerlynx vs 11.8 months with placebo.

Recommendation: Nerlynx ® be non-preferred.

Clinical Criteria: Clinical PA required for appropriate diagnosis

Tecentriq® (atezolizumab); PDL category- Cancer

Atezolizumab, the active ingredient of Tecentriq®, is an Fc-engineered, humanized, monoclonal antibody that binds to PD-L1 and blocks its interactions with the PD-1 and B7.1 receptors. It is a non-glycosylated IgG1 kappa immunoglobulin. PD-L1 may be expressed on tumor cells and/or tumor-infiltrating immune cells and can contribute to the inhibition of the anti-tumor immune response in the tumor microenvironment. Binding of PD-L1 to the PD-1 and B7.1 receptors found on T cells and antigen presenting cells suppresses cytotoxic T-cell activity, T-cell proliferation and cytokine production. It is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who: Are not eligible for cisplatin-containing chemotherapy, or Have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy. 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 confirmatory trials. For the treatment of patients with metastatic non-small cell lung cancer (NSCLC) who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Tecentriq®. The efficacy of Tecentriq® was assessed in one multicenter, open-label, single-arm study that included patients with locally advanced or metastatic urothelial carcinoma who were ineligible for cisplatin-containing chemotherapy and were previously untreated or had disease progression at least 12 months after neoadjuvant or adjuvant chemotherapy.

Recommendation: Tecentriq ® be non-preferred.

Clinical Criteria: Clinical PA required for appropriate diagnosis. Tecentriq; For the treatment of patients with metastatic non-small cell lung cancer (NSCLC) who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Tecentriq®.

Verzenio® (abemaciclib); **PDL category**- Cancer

Abemaciclib, the active ingredient of Verzenio® is a kinase inhibitor, an inhibitor of cyclin-dependent kinases 4 and 6 (CDK4 and CDK6). In breast cancer xenograft models, abemaciclib dosed daily without interruption used as monotherapy or in combination with anti-estrogens resulted in reduction of tumor size. It is indicated in combination with fulvestrant for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease

progression following endocrine therapy AND as monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting. Dose modifications may be required for cases of adverse events, drug interactions, or with severe hepatic impairment. Verzenio® in combination with fulvestrant was found to be significantly more effective than placebo plus fulvestrant for progression-free survival.

Recommendation: Verzenio ® be non-preferred.

Clinical Criteria: Clinical PA required for appropriate diagnosis.

Armonair® Respiclick (fluticasone propionate); **PDL category**- Antiastmatic-Steroid Inhalants

Fluticasone propionate, the active ingredient of Armonair® Respiclick, is a synthetic trifluorinated corticosteroid with anti-inflammatory activity. Fluticasone propionate has been shown in vitro to have a binding affinity for the human glucocorticoid receptor that is 18 times that of dexamethasone, almost twice that of beclomethasone-17-monopropionate, and over 3 times that of budesonide. Corticosteroids have been shown to have a wide range of actions on multiple cell types (e.g. mast cells, eosinophils) and mediators (e.g. histamine and leukotrienes) involved in inflammation. These anti-inflammatory actions of corticosteroids contribute to the efficacy in asthma. Indicated for the maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older. Armonair® Respiclick is not indicated for the relief of acute bronchospasm. Recommended dose is to rinse Rinse the mouth with water without swallowing after each dose. Administer 1 inhalation orally twice daily. Priming of the inhaler is not needed and it should not be used with a spacer or volume holding chamber. The safety and efficacy of Armonair® Respiclick were assessed in 2 confirmatory trials of 12 weeks duration, a 26 week safety trial, and 2 dose-ranging trials.

Recommendation: Armonair® Respiclick be non-preferred.

Clinical Criteria: All step 5 medications need to be tried before moving to step 8's. Dosing limits apply to whole category, please see dosage

Fiasp® (insulin aspart); **PDL category**- Diabetic- Insulin

Insulin aspart, the active ingredient of Fiasp®, is a rapid-acting insulin analog for SC or IV use to lower blood glucose. It is produced by recombinant DNA technology. It indicated to improve glycemic control in adults with diabetes mellitus. The safety and efficacy of Fiasp® added to insulin detemir in patients with type 1 DM inadequately controlled at baseline were assessed in a randomized, active-controlled, multicenter 26-week study. Individualize the dose based on the patient's metabolic needs, blood glucose monitoring results, and glycemic control goal. Dose adjustments may be needed when switching from another insulin, with changes in physical activity, changes in concomitant medications, changes in meal patterns, changes in renal or hepatic function, or during acute illness to minimize the risk of hypoglycemia or hyperglycemia. Not for IM use or to be diluted or mixed with other insulin or solution, except infusion fluids. The safety and efficacy of Fiasp® added to insulin detemir in patients with type 1 DM inadequately controlled at baseline were assessed in a randomized, active-controlled, multicenter 26-week study (N=1143). Adults were randomized to either blinded mealtime Fiasp®, blinded mealtime Novolog®, or open-label post-meal Fiasp®, all in combination with once or twice daily insulin detemir. Mealtime Fiasp® or Novolog® was injected 0-2 minutes before the meal and post-meal Fiasp® was injected 20 minutes after the start of the meal. Results suggested that after 26

weeks of treatment, treatment difference in HbA1c reduction from baseline between mealtime Fiasp® compared to mealtime Novolog®, and the treatment difference between post-meal Fiasp® compared to mealtime Novolog®, met the pre-specified non-inferiority margin (0.4%). Insulin doses were similar between groups at baseline and at the end of the trial. Results can be seen in the table below, which was adapted from the prescribing information.

Recommendation: Fiasp ® be non-preferred.

Clinical Criteria: none

Mydayis® (dextroamphetamine & amphetamine (mixed salt amphetamine)); **PDL category**- Stimulants-Long Acting Amphetamines Salt

Mydayis® contains mixed salts of a single-entity amphetamine, a central nervous system (CNS) stimulant. Mydayis® capsules contains equal amounts of 4 salts: dextroamphetamine sulfate, amphetamine sulfate, dextroamphetamine saccharate, and amphetamine aspartate monohydrate. This results in a 3:1 mixture of dextro- to levo- amphetamine base equivalent. While the exact mechanism of action is not known, it is thought amphetamines work 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. Mydayis® 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 patients 13 years and older. Pediatric patients 12 years and younger experienced higher plasma exposure than patients 13 years and older at the same dose, and experienced higher rates of adverse reactions, mainly insomnia and decreased appetite. As the effects of Mydayis® may last up to 16 hours and there is potential for insomnia, administer once daily in the morning upon awakening with or without food.

Recommendation: Mydayis ® be non-preferred.

Clinical Criteria: For the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 13 years and older. The concomitant use of Mydayis® is contraindicated with monoamine oxidase inhibitors (MAOIs) or within 14 days after discontinuing MAOI treatment, as concomitant use can increase hypertensive crisis.

Symproic® (naldemedine); **PDL category**- GI, Misc

Naldemedine, the active ingredient of Symproic®, is an opioid antagonist with binding affinities for mu-, delta- and kappa-opioid receptors. It functions as a peripherally-acting mu-opioid receptor antagonist in tissues, such as the GI tract, thus decreasing the constipating effects of opioids. Naldemedine is a derivative of naltrexone to which a side chain has been added that reduces its ability to cross the blood-brain barrier. It is also a substrate of P-gp efflux transporter. Overall, per its properties, the CNS penetration of naldemedine is expected to be negligible at the recommended dose levels, thus limiting the potential for interference with centrally-mediated opioid analgesia. It is indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g. weekly) opioid dosage escalation. The safety and efficacy of Symproic® were assessed in two replicate, 12-week, randomized, double-blind, placebo-controlled studies where Symproic® was used without laxatives in adults with opioid induced constipation (OIC) and chronic

non-cancer pain receiving a stable opioid morphine equivalent daily dose of at least 30mg for at least 4 weeks before enrollment.

Recommendation: Symproic ® be non-preferred.

Clinical Criteria: For the treatment of Opioid Induced Constipation(OIC).

Trelegy Ellipta® (fluticasone furoate, umedlidinium, & vilanterol); **PDL category**- Antiasthmatic-Adrenergic

Trelegy® Ellipta is an inhalation powder that includes a combination of 3 drugs from 3 different classes of medication, including fluticasone furoate (a corticosteroid), umeclidinium (a long-acting muscarinic antagonist, often referred to as an anticholinergic), and vilanterol (a long-acting beta2 agonist or LABA). It is indicated for the the long-term, once-daily, maintenance treatment of patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, who are on a fixed-dose combination of fluticasone furoate and vilanterol for airflow obstruction and reducing exacerbations in whom additional treatment of airflow obstruction is desired or for patients who are already receiving umeclidinium and a fixed-dose of fluticasone furoate and vilanterol. Trelegy® Ellipta is not indicated for the relief of acute bronchospasm or for the treatment of asthma. Vilanterol should be used with extreme caution in patients being treated with monoamine oxidase inhibitors, TCAs, or drugs known to prolong the QTc interval or within 2 weeks of discontinuation of such agents.

Recommendation: Trelegy Ellipate® be non-preferred.

Clinical Criteria: Remove comment: ADVAIR DISKUS- Patients currently using Advair Diskus® will have a 90 day grace period to transition to Advair HFA® or another preferred product on the PDL such as Dulera® or Symbicort. Update criteria with: 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.

Benlysta® (belimumab); **PDL category**- Systemic Lupus Erythematosus

Belimumab, the active ingredient of Benlysta®, is a human IgG1 lambda monoclonal antibody specific for soluble human B lymphocyte stimulator protein (BLyS). It is a BLyS-specific inhibitor that blocks the binding of soluble BLyS, a B-cell survival factor, to its receptor on B cells. Benlysta® does not bind B cells directly, but by binding BLyS, Benlysta® inhibits the survival of B cells, including autoreactive B cells, and reduces the differentiation of B cells into immunoglobulin-producing plasma cells. Indicated for the treatment of adults with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy. The efficacy of Benlysta® has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. It has not been studied in combination with other biologics or intravenous cyclophosphamide. Use of Benlysta® is not recommended in these situations. The safety and efficacy of Benlysta® IV plus standard therapy were assessed in 3 randomized, double-blind, placebo controlled trials (N=2,133) that included adults with SLE. The stable standard therapy was comprised of any of the following, alone or in combination: corticosteroids, antimalarials, NSAIDs, and immunosuppressives. Patients with severe active lupus nephritis and severe active CNS lupus were excluded from the trials. All patients had a Safety of Estrogens in Lupus Erythematosus National Assessment- SLE Disease Activity

Index (SELENA-SLEDAI) score of ≥4 at baseline and a history of autoantibodies, but 28% was autoantibody negative at baseline. The co-primary endpoints were the % change in SELENA-SLEDAI score at week 24 and time to first flare over 52 weeks. Significant differences were not seen between any Benlysta® dose and placebo. Exploratory sub-group analyses of SRI-4 response rate in black patients (N=91) were performed. The SRI-4 response rate was slightly higher in black patients receiving Benlysta® vs placebo (45% vs 39%), but the treatment difference was not as large as that seen in the overall population and no definitive conclusion can be drawn from this subgroup analysis. It is recommended to use caution when considering treatment with Benlysta® in black/African-American patients. The probability of experiencing a severe SLE flare was also calculated in this study. The proportion reporting at least 1 severe flare during the study was lower with Benlysta® compared with placebo (11% vs 18%).

Recommendation: Benlysta ® be non-preferred.

Clinical Criteria: Approvals will require previous trial of corticosteroids, antimalarials, NSAIDS and immunosuppressives.

Endari® (L-glutamine); **PDL category**- Miscellaneous

L-glutamine, the active ingredient of Endari®, is an amino acid. The mechanism of action of using L-glutamine for treating sickle cell disease (SCD) is not fully understood. Sickle red blood cells are more susceptible to oxidative damage than normal red blood cells, which may contribute to the chronic hemolysis and vaso-occlusive events associated with SCD. The pyridine nucleotides, NAD+ and its reduced form NADH, play roles in regulating and preventing oxidative damage in red blood cells. L-glutamine may improve the NAD redox potential in sickle red blood cells through increasing the availability of reduced glutathione. It is indicated to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older. Administer PO BID, based on weight. The safety and efficacy of Endari® were assessed in a randomized, double-blind, placebo-controlled, multicenter study that included patients (N=230) ages 5 to 58 years with sickle cell anemia or sickle β-thalassemia who had 2 or more painful crises within 12 months prior to enrollment. Eligible patients stabilized on hydroxyurea for at least 3 months continued therapy throughout the study. The trial did exclude patients who had received blood products within 3 weeks, had renal insufficiency or uncontrolled liver disease, were pregnant, or were lactating. Treatment was continued for 48 weeks.

Recommendation: Endari ® be non-preferred.

Clinical Criteria: Evidence of other preferred L-glutamine products utilization and reason for failure.

Haegarda® (C1 esterase inhibitor); **PDL category**- Hereditary Angioedema

Haegarda® is a human plasma-derived, purified, pasteurized, lyophilized concentrate of C1 Esterase Inhibitor (C1-INH) to be reconstituted for subcutaneous (SC) administration. The manufacturing process for Haegarda® includes several steps to reduce the risk of virus transmission. C1-INH is a normal constituent of human plasma and belongs to the group of serine protease inhibitors that includes antithrombin III, alpha1-protease inhibitor, alpha2-antiplasmin, and heparin cofactor II. C1-INH has an important inhibiting potential on several major human cascade systems, including the complement, fibrinolytic and coagulation systems. C1-INH is generally activated during the inflammatory process and inactivates its substrate by covalently binding to the reactive site. C1-INH is the only known inhibitor for the C1r and C1s subcomponents of the complement

component 1 (C1), coagulation factor XIIa and plasma kallikrein. Also, C1-INH is the main inhibitor for coagulation factor XIa. It is indicated for routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients. The safety and efficacy of Haegarda® were assessed in a multicenter, randomized, double-blind, placebo-controlled crossover study that included adults and adolescents (N=90) with symptomatic HAE type I or II. The results suggested that both doses of Haegarda® resulted in a significant difference in the time-normalized number of HAE attacks (the rate of attacks) relative to placebo.

Recommendation: Haegarda ® be non-preferred.

Clinical Criteria: Haegarda is indicated for routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients

Parsabiv® (etelcalcetide); **PDL category**- Calcimimetic Agents

Etelcalcetide, the active ingredient of Parsabiv®, is a synthetic peptide calcium-sensing receptor agonist. It is a calcimimetic agent that allosterically modulates the calcium-sensing receptor (CaSR). Etelcalcetide binds to the CaSR and enhances activation of the receptor by extracellular calcium. Activation of the CaSR on parathyroid chief cells decreases parathyroid hormone (PTH) secretion. It is indicated for the treatment of secondary hyperparathyroidism (HPT) in adults with chronic kidney disease (CKD) on hemodialysis. Parsabiv® has not been studied in adults with parathyroid carcinoma, primary hyperparathyroidism, or with chronic kidney disease who are not on hemodialysis and is not recommended for use in these populations. The safety and efficacy of Parsabiv® for the treatment of secondary hyperparathyroidism in patients with CKD receiving hemodialysis were assessed in 2 randomized, double-blind, placebo-controlled, 26-week studies. In both studies, the primary outcome measure was the proportion of patients with a greater than 30% reduction in PTH levels from baseline to the efficacy assessment phase (mean PTH levels for weeks 20 through 27, inclusive). The other outcome measures were the proportion of patients with a mean PTH ≤300pg/mL, the percent change from baseline in PTH, corrected serum calcium, and phosphate levels.

Recommendation: Parsabiv ® be non-preferred.

Clinical Criteria: Parsabiv is for the treatment of secondary hyperparathyroidism (HPT) in adults with chronic kidney disease (CKD) on hemodialysis. Parsabiv® has not been studied in adults with parathyroid carcinoma, primary hyperparathyroidism, or with chronic kidney disease who are not on hemodialysis and is not recommended for use in these populations.

Vabomere® (meropenem- vaborbactam); **PDL category**- Anti-Infective Combo's- Misc

Vabomere® is a combination drug that contains meropenem (a synthetic penem antibacterial drug) and vaborbactam (a cyclic boronic acid beta-lactamase inhibitor). The bactericidal action of meropenem results from the inhibition of cell wall synthesis. The vaborbactam component is a non-suicidal beta-lactamase inhibitor that protects meropenem from degradation by certain serine beta-lactamases, such as *Klebsiella pneumoniae* carbapenemase. Vaborbactam does not have any antibacterial activity and does not decrease the activity of meropenem against meropenem-susceptible organisms. It is indicated for the treatment of patients 18 years of age and older with complicated urinary tract infections (cUTI) including pyelonephritis caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae species* complex. The safety and efficacy of Vabomere® were assessed in a randomized,

double-blind, double-dummy multicenter study that included adults with cUTI, including pyelonephritis (N=545). Patients were randomized to Vabomere® IV or with piperacillin/tazobactam IV, and switch to an oral antibacterial agent such as levofloxacin was allowed after a minimum of 15 doses of IV therapy. Overall, in both treatment groups, 59% had pyelonephritis and 40% had cUTI, with 21% and 19% having a non-removable and removable source of infection, respectively. Mean duration of IV treatment in both groups was 8 days and mean total treatment duration (IV and oral) was 10 days.

Recommendation: Vabomere® be non-preferred.

Clinical Criteria: For the treatment of patients ≥ 18 years of age and 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.

Xatmep® (methotrexate); **PDL category**- Rheumatoid Arthritis

Methotrexate, the active ingredient of Xatmep®, is a folate analog metabolic inhibitor. It inhibits dihydrofolic acid reductase and interferes with DNA synthesis, repair, and cellular replication. The mechanism of action in polyarticular juvenile idiopathic arthritis is not known, but it may affect immune functions. It is indicated for the treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as part of a multi-phase, combination chemotherapy maintenance regimen AND in the management of pediatric patients with active polyarticular juvenile idiopathic arthritis (pJIA) who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).

Recommendation: Xatmep ® be non-preferred.

Clinical Criteria: Treatment failure or intolerance to other forms of preferred methotrexate.

Ximino® (minocycline hydrochloride, extended-release); **PDL category**- Tetracyclines

Minocycline, the active ingredient of Ximino®, is a semi-synthetic derivative of tetracycline. The exact mechanism of action of use for the treatment of acne is not known. It is indicated to treat only inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, Ximino® should be used only as indicated. Ximino® did not demonstrate any effect on non-inflammatory acne lesions. The safety of Ximino® has not been established beyond 12 weeks of use. This formulation of minocycline has not been evaluated in the treatment of infections. Ximino® is not bioequivalent to immediate release minocycline products. Another minocycline extended-release formulation is available which is bioequivalent to Ximino®. Take approximately 1mg/kg once daily for 12 weeks. Higher doses have not shown to be of additional benefit in the treatment of inflammatory lesions of acne, and may be associated with more acute vestibular side effects. The safety and efficacy of minocycline hydrochloride for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris were assessed in 2 double-blind, randomized, multicenter, placebo-controlled 12-week studies that include subjects ≥12 years of age. The two primary efficacy endpoints were the mean percent change in inflammatory lesion counts from baseline to 12

weeks and the percentage of subjects with an Evaluator's Global Severity Assessment (EGSA) of clear or almost clear at 12 weeks.

Recommendation: Ximino ® be non-preferred.

Clinical Criteria: none.

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: 4:30PM

The next meeting will be held on **March 12, 2017** 5:30pm –8:30pm at the Augusta Armory.