Department of Vermont Health Access
Pharmacy Benefit Management Program
DUR Board Meeting Minutes
December 04, 2018

Board Members:

Present:

Bill Breen, RPh
Zail Berry, MD
Joseph Nasca, MD
Jocelyn Van Opdorp, PharmD
Clayton English, PharmD
Louise Rosales, NP
Renee Mosier, PharmD
Claudia Berger, MD

Absent: Patricia King, MD

Staff:

Jason Pope, DVHA
Laurie Brady, RPh, Change HealthCare
Nancy Hogue, PharmD, DVHA
Carrie Germaine, DVHA
Scott Strenio, MD, DVHA
Jeffrey Barkin, MD Change Healthcare
Lisa Hurteau, PharmD, DVHA
Mike Ouellette, RPH, Change Healthcare

Guests:

Linda Burns, Abbott
Franco Casagrande, Abbvie
Maggie Glassman, Alkermes
Lisa Libera, Teva
Michael Approlin, J and J
Karen Phillips, Amgen
Timothy Birner, Alermes
Hannah Parker, Amgen
Megan Walsh, Abbvie
Robert Shapiro, UVM Medical Center
Karen Brownstein
Alex Felizardo, Otsuka
Jessica Kreitzman, Amgen

1. Executive Session:

- An executive session was held from 6:00 p.m. until 6:25 p.m.

2. Introductions and Approval of DUR Board Minutes:

- Introductions were made around the table.
- The October meeting minutes were accepted as printed.

3. DVHA Pharmacy Administration Updates: Nancy Hogue, PharmD, DVHA and Lisa Hurteau, PharmD, DVHA

- DVHA is Working on finding a new meeting location for 2019. The current Williston facility will not be available after January.
- Lisa Hurteau gave an overview of the Cost Control Report which discusses clinical and cost strategies to manages drug utilization and spend. This is a public document, and a link will be sent to the board for review.

4. Medical Director Update: Scott Strenio, MD, DVHA

- There will be a new DHVA Website that will enable providers to choose which kind of updates they would like to receive. The goal is for this to launch in the spring.
- DVHA is developing best practices for urine drug testing.

5. Follow-up Items from Previous Meetings: Laurie Brady, RPh, Change Healthcare

- Add the subcategory Calcitonin gene-related peptide (CGRP) Inhibitors to the Anti-migraine Agents category.
- Add Aimovig™ (erenumab-aooe) to non-preferred.
    - Clinical criteria
        - **Aimovig:** The patient is 18 years of age or older AND patient has a diagnosis of episodic migraine (4-14 headache days per month with migraine lasting 4 hours or more) or chronic migraine (≥ 15 headache days per month, of which ≥ 8 are migraine days, for at least 3 months) AND patient has failed or has a contraindication to an adequate trial (≥ 60 days) of at least TWO medications for migraine prophylaxis from at least 2 different classes (tricyclic antidepressants, SNRI's, beta-blockers, or anticonvulsants). Initial approval will be granted for 6 months. For re-approval after 6 months, the patient must have documentation of a decrease in the number of headache days per month or decreased use of acute migraine medications such as triptans. Pharmacy claims will also be evaluated to assess compliance with the medication. Note: Aimovig approvals for 140mg dose(s) must use "140DOSE" package (containing 2 x 70mg syringes or auto-injectors). Approval will not be granted for 2 separate 70mg packages.

Public Comments: Dr. Robert Shapiro from UVM Medical Center: Thanked the board for taking the time and consideration to re-review the Aimovig criteria.

Board Decision: The Board unanimously approved the above recommendation.

6. RetroDUR/DUR: Laurie Brady, RPh, Change Healthcare, Michael Ouellette, RPH, Change Healthcare, and Jeffrey Barkin, MD, Change Healthcare

- **Discuss Prospective DUR Edits**

ProDUR is an integral part of the Vermont Medicaid claims adjudication process. ProDUR includes:

- reviewing claims for therapeutic appropriateness before the medication is dispensed
- reviewing the available medical history
- focusing on those patients at the highest severity of risk for harmful outcome
- intervening and/or counseling when appropriate

Prospective Drug Utilization Review (ProDUR) encompasses the detection, evaluation and counseling components of pre-dispensing drug therapy screening. The ProDUR system addresses situations in which potential drug problems may exist. ProDUR performed prior to dispensing assists pharmacists in ensuring that patients receive appropriate medications. This is accomplished by providing information to the dispensing pharmacist that may not have been previously available.

Because ProDUR examines claims from all participating pharmacies, drugs which interact or are affected by previously dispensed medications can be detected. While the pharmacist uses his/her education and professional judgment in all aspects of dispensing, ProDUR is intended an informational tool to aid the pharmacist.

The following ProDUR Reason of Service types will deny for the Vermont Medicaid program:

- Drug-to-Drug Interaction (Highest Severity Levels)
- Therapeutic Duplication

ProDUR Edits that deny may be overridden at the Pharmacy Point of Sale (POS) using the interactive NCPDP DUR override codes. When a claim is rejected for a DUR edit, pharmacies may override the denial by submitting the appropriate Professional Service and Result of Service codes. The designated Professional Service code must accompany the appropriate Result of Service code as indicated in the chart to allow the override.

The valid DUR Reason for Service Codes for Vermont Medicaid are:
DD - Drug-Drug Interaction
TD - Therapeutic Duplication

The only acceptable Professional Service Codes are:
MR – Medication Review
M0 – Prescriber Consulted
R0 – Pharmacist Consulted Other

Recommendation: Change Healthcare will email the complete document to the DUR board members.

Public Comment: No public comment.

Board Decision: None needed.

- **Introduction: Sildenafil Use**

Sildenafil, a phosphodiesterase-5 inhibitor, has been shown to be an effective treatment in Type I pulmonary hypertension, as monotherapy or in combination with other classes of medications (prostanoids, endothelin receptor antagonists, soluble guanylate cyclase stimulants, calcium channel blockers). The SUPER-1 trial looked at 277 patients with PAH type 1 who were given sildenafil at doses of 20mg, 40mg or 80mg TID compared with placebo for 12 weeks. Improvements in pulmonary hemodynamics and performance of the 6-minute walk test were seen at 12 weeks and the effects persisted for at least one year. The effects on mortality, however, are unknown. Also uncertain is whether sequential single agent therapy or combination therapies are the better strategy for improving outcomes and decreasing mortality.

Sildenafil is also an effective medication for treating erectile dysfunction, by increasing nitric oxide mediated increase in cGMP. The dosing is typically 50mg per day, although the dose can be titrated from 25mg to 100mg. The dosing for PAH is 20-80mg three time daily.

Effective 7/1/06, phosphodiesterase-5 (PDE-5) inhibitors were excluded from coverage for all Vermont Pharmacy Programs for the treatment of erectile dysfunction. This was resultant from changes set into effect January 1, 2006, and as detailed in Section 1903 (i)(21)(K) of the Social Security Act (the Act), precluding Medicaid Federal Funding for outpatient drugs used for the treatment of sexual or erectile dysfunction.

Change Healthcare will use paid, non-reversed Medicaid pharmacy claims from calendar year 2016 and compare them with those of calendar year 2017, when sildenafil became a preferred drug, excluding members with Part D, VMAP and Healthy Vermonters coverage. They will identify members with at least one prescription for sildenafil (Viagra and Revatio) and evaluate the dosage, frequency of administration, regularity and frequency of fills. Change Healthcare will then evaluate whether there is compliance in the treatment of PAH or possible surreptitious use for erectile dysfunction, a non-covered condition.

Recommendation: None at this time.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation with the addition of including the 1st half of 2018 in the analysis.

- **Data presentation: Vivitrol Adherence**

The opioid epidemic has resulted in a dramatic increase in the use of abuse deterrent medications, the most common being the agonist/antagonist combination of buprenorphine and naloxone, given in an oral form daily. For patients who are not adherent to a daily oral dose of abuse deterrent medications, there are depot intramuscular formulations of buprenorphine and naltrexone, each given once every 28 days. Two recent trials comparing daily sublingual buprenorphine with monthly LAI naltrexone found minimal differences in abstinence rates but may offer advantages for patients who do not respond to agonist treatment, cannot adhere to a daily medication, or are in a safety-sensitive occupation that does not permit concurrent agonist treatment. However, trials of LAI naltrexone have been limited by high dropout rates and the transition on to LAI naltrexone may be a challenge for some patients. As an example, a 2011 trial compared a once-monthly, injectable depot formulation of naltrexone with placebo in 250 patients with a DSM-IV diagnosis of opioid dependence over 24 weeks, finding that the median proportion of weeks of confirmed abstinence was greater in the actively treated group compared with the placebo group (90 versus 35 percent); however, these findings excluded 47 percent of the patients who did not complete the study. Treatment with oral or
LAI naltrexone is a reasonable first-line alternative to methadone or buprenorphine in those who have a mild opioid use disorder, require medical supervision or are in occupations where opioid agonist treatment is not allowed (public safety, transport of hazardous materials, etc.).

Change Healthcare used paid, non-reversed Medicaid pharmacy and medical claims date from SFY 2016 and 2017, excluding members with Part D, VMPA and Healthy Vermont coverage. They identified members given at least one dose of IM naltrexone and looked to see how many consecutive doses were given monthly, without any interruption. They followed each member out from the first prescription to the end of calendar year 2017, allowing us to assess the percentage of members who were adherent with therapy.

There were 325 members who were prescribed at least one dose of IM naltrexone.

Members with diagnosis of Etoh abuse = 50
Members with diagnosis of Opiate abuse= 116
Members with both diagnoses= 156
Members with neither diagnosis=3

# Fills	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	20	22
# Member	129	41	32	24	19	21	8	9	8	9	5	3	2	1	4	4	1	2	1	2
# of Pts with Alcohol dependence dx	23	5	6	3	0	1	2	0	1	2	3	1	1	0	0	0	0	0	0	2
# of Pts with Opioid dependence dx	41	15	14	7	9	7	3	5	3	3	2	1	0	1	2	2	0	1	0	0
# of Pts with both dx	63	20	12	14	10	13	3	4	4	4	0	1	1	0	2	2	1	1	1	0
# of Pts with neither dx	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

40 members were transitioned to a buprenorphine containing product after last fill of IM naltrexone, and no members were transitioned to methadone. Most members with multiple fills of Vivitrol had any appropriate interval between fills and were consistent in getting the injection on a regular basis. There were some members, mostly in the 2-fill category, who had long intervals between the first and second injection. Of the 72 members who had less than 24 days between the first and second fills, 16 had different providers for the first and second fills. Of the 236 members who had greater than 36 days between the first and second fills, 57 had different providers for the first and second fills. The prescribers that were different for a given patient often came from the same practice. There were 2 practices that cared for the majority of the members.

Recommendation: None at this time.

Public Comment: None at this time.

Board Decision: The Board requested that Change Healthcare re-run the data only for patients with continuous eligibility from the 1st dose through the end of the analysis time frame.

7. Clinical Update: Drug Reviews: Jeffrey Barkin, MD and Laurie Brady RPh, Change Healthcare

Abbreviated New Drug Reviews:

- None at this time.

Full New Drug Reviews:

a) Aristada® Initio (aripiprazole lauroxil, extended-release injection)

Aripiprazole lauroxil, the active ingredient of Aristada® Initio, is an atypical antipsychotic and a prodrug of aripiprazole. While the exact mechanism of action of aripiprazole is not known, it is thought its efficacy is mediated through a combination of partial agonist activity at dopamine D2 and serotonin 5-HT1a receptors, and antagonist activity at 5-HT2A receptors. Actions at other receptors could explain some of the adverse reactions of aripiprazole (e.g.

orthostatic hypotension due to antagonist activity at adrenergic alpha1 receptors). It is indicated for use in combination with with oral aripiprazole, it is indicated for the initiation of Aristada® when used for the treatment of schizophrenia in adults. The efficacy of Aristada® Initio, in combination with oral aripiprazole, for the initiation of Aristada® when used for the treatment of schizophrenia in adults, was established by adequate and well-controlled studies of oral aripiprazole and Aristada® in adults with schizophrenia (per studies in Aristada® prescribing information) and a single pharmacokinetic bridging study. The efficacy of Aristada® was established, in part, on the basis of efficacy data from the clinical trials of the oral aripiprazole formulation when used for the treatment of schizophrenia. In addition to the oral studies, the efficacy of Aristada® was established in a 12-week, randomized, double-blind, placebo-controlled study in adult patients with schizophrenia.

Recommendation:

- Add Aristada Initio™ to preferred.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendation.

b) Firvanq® (vancomycin hydrochloride powder for oral solution)

Vancomycin, the active ingredient of Firvanq®, is a tricyclic glycopeptide antibiotic derived from *Amycolatopsis orientalis*. The bactericidal action of vancomycin against the vegetative cells of *C. difficile* and *S. aureus* results mainly from inhibition of cell-wall biosynthesis. Also, vancomycin alters bacterial-cell-membrane permeability and RNA synthesis. It is indicated for the treatment of *Clostridium difficile*-associated diarrhea in adults and pediatric patients less than 18 years of age and for the treatment of enterocolitis caused by *Staphylococcus aureus* (including methicillin-resistant strains) in adults and pediatric patients less than 18 years of age. Parenteral administration of vancomycin is not effective for the above indications; therefore, vancomycin must be given orally for these infections. Orally administered vancomycin HCl is not effective for treatment of other types of infection. Prior to oral administration, the supplied Firvanq® powder must be reconstituted by the healthcare provider (i.e. a pharmacist) to produce the oral solution. There were 2 clinical trials that assessed the efficacy of vancomycin 125mg PO QID for

10 days in adults with *C. difficile*-associated diarrhea (CDAD). Adults included in the studies received no more than 48 hours of treatment with oral vancomycin or oral/IV metronidazole in the 5 days preceding enrollment.

Recommendation:

- Add Firvanq™ (vancomycin HCl) powder for oral solution to non-preferred with Quantity Limit = 1 bottle (150ml) per course of therapy. If more than 150ml is required, use of 300ml bottle is required.
  - Clinical criteria
    - Revise Criteria for Approval (all oral Vancomycin products)**:** patient's diagnosis or indication is enterocolitis caused by Staphylococcus aureus OR patient's diagnosis or indication is antibiotic associated pseudomembranous colitis caused by Clostridium AND For approval of brand Vancocin, the patient must meet the above criteria and have a documented intolerance to the generic.

Public Comments: None at this time.

Board Decision: The Board unanimously approved the above recommendation.

c) Jynarque® (tolvaptan)

Tolvaptan, the active ingredient of Jynarque®, is a selective vasopressin V2-receptor antagonist, with an affinity for the V2-receptor that is 1.8 times that of native arginine vasopressin (AVP). Tolvaptan affinity for the V2-receptor is 29 times that for the V1a-receptor. In human cyst epithelial cells, tolvaptan inhibited AVP-stimulated in vitro cyst growth and chloride-dependent fluid secretion into cysts. It is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD). Jynarque® has a box warning regarding the increased risk of serious livery injury, as it can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported. It is recommended to measure ALT, AST, and bilirubin before starting treatment, at 2 weeks and 4 weeks after initiation, then monthly for the first 18 months and every 3 months thereafter. Prompt action in response to laboratory abnormalities, signs or symptoms indicative of hepatic injury can mitigate the risk of serious hepatoxicity. Due to the risks of serious liver injury, Jynarque® is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS)

called the Jynarque® REMS Program. Jynarque® was shown to slow the rate of decline in renal function in patients at risk of rapidly progressing ADPKD in 2 trials, including the TEMPO 3:4 study that included patients at earlier stages of disease and the REPRISE study that included patients at later stages.

Recommendation:

- Add a new PFL category Vasopressin Receptor Antagonists.
- Add Jynarque® tablets (tolvaptan) with Quantity Limit = 56 tablets/28 days to non-preferred.
- Move Samsca® tablets (tolvaptan) with Quantity limit = 15 mg tablets (1 tablet/day), 30 mg tablets (2 tablets/day) out of Misc category into new Vasopressin Receptor Antagonist category.
    - Clinical criteria
        - Add **Jynarque:** The patient must be ≥ 18 years of age AND the patient is at risk of rapidly progressing Autosomal Polycystic Kidney Disease (ADPKD) AND the patient has normal serum sodium concentrations before starting the medication (results must be submitted) AND the patient and provider are enrolled in the Jynarque® REMS program

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

d) Kapspargo® (metoprolol succinate capsules, extended-release)

Metoprolol succinate, the active ingredient of Kapspargo®, is a beta1-selective (cardioselective) adrenergic receptor blocking agent. At higher plasma concentrations though, metoprolol also inhibits beta2-adrenoreceptors, mainly located in the bronchial and vascular musculature. The proposed mechanism of action in hypertension include competitive antagonism of catecholamines at peripheral adrenergic neuron site leading to decreased cardiac output, a central effect leading to reduced sympathetic outflow to the periphery, and suppression of renin activity. For angina, by blocking catecholamine-induced increases in heart rate, in velocity and extent of myocardial contraction, and in blood pressure, metoprolol reduces the oxygen needs of the heart at any given level of effort, thus making it useful in the long-term management of angina. The exact mechanism of action with heart failure is not known. It is indicated for: The treatment of hypertension, to lower blood pressure; may be administered with other antihypertensive agents, the long-term treatment of angina pectoris, to reduce angina attacks and to improve exercise tolerance and

Reducing the risk of cardiovascular mortality and heart-failure hospitalization in patients with heart failure. Studies in the prescribing information were those with metoprolol succinate. One double-blind study included patients with mild to moderate hypertension (N=1092) who were randomized to metoprolol succinate (25mg, 100mg or 400mg), Plendil®, the combination or placebo. After 9 weeks, the metoprolol group decreased sitting blood pressure by 6-8mmHg/4-7mmHg (placebo-corrected change from baseline) at 24 hours post-dose. The combination of metoprolol succinate with Plendil® had greater effects on blood pressure.

Recommendation:

- Add Kapspargo Sprinkle™ (metoprolol succinate XL) to non- preferred.
  - Clinical criteria
    - Add **Kapspargo:** patient is unable to take a solid oral dosage form and has a treatment failure with an immediate release oral solution or crushed tablets.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

e) Lucemyra® (lofexidine)

Lofexidine, the active ingredient of Lucemyra®, is a central alpha-2 adrenergic agonist that binds to receptors on adrenergic neurons. This reduces the release of norepinephrine and decreases sympathetic tone. It is indicated for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults. There were 2 randomized, double-blind placebo-controlled studies to assess the safety and efficacy of Lucemyra®. In clinical studies, it was found to significantly reduce the SOWS-Gossop total score as compared with placebo, and a significantly larger number of subjects completed treatment with Lucemyra® as compared with placebo. Lofexidine has been available in Europe for many years and as a result there have been several studies comparing it to clonidine for both efficacy and safety. A Cochrane review summarized the available data and concluded that lofexidine and clonidine were similarly effective (moderate level of evidence) but that lofexidine was better tolerated and associated with fewer adverse effects, especially less hypotension (low quality of evidence).

Recommendation:

- Add the sub-category Opiate Withdrawal Treatment to Opiate Dependency category.
  - Add **Central Alpha Agonists** Clonidine IR tablets (compare to Catapres®) and **Note:** Methadone for opiate dependency or

withdrawal can only be prescribed through a Methadone Maintenance Clinic to preferred.
- Add Lucemyra® (lofexidine) with Maximum length of therapy = 14 days to non-preferred.
- Clinical criteria
  - Add **Lucemyra**: Indication for use is the mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation AND the patient is ≥ 18 years of age AND the patient is unable to tolerate clonidine due to significant side effects.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

f) Olumiant® (baricitinib)

Baricitinib, the active ingredient of Olumiant®, is a Janus Kinase (JAK) Inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membranes to influence cellular processes of hematopoiesis and immune cell function. It is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies. Use in combination with other JAK inhibitors, biologic disease-modifying antirheumatic drugs (DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended. A 2017 double-blind, placebo- and active-controlled phase 3 study in the NEJM by Taylor et al[2] suggested that baricitinib 4mg was significantly more effective as compared with placebo for the primary endpoint of the proportion achieving an ACR20 response at week 12 (70% vs 40%, respectively; $p<0.001$). In addition, baricitinib 4mg was found to be non-inferior to adalimumab at week 12 for ACR response and per the statistical analysis plan, baricitinib was considered to be significantly superior to adalimumab (70% vs 61%, respectively; $p=0.014$). The FDA, however, approved only the 2 mg/day dose due to concerns about the risk of thrombotic events seen with the higher dose. There is no evidence to support that the approved 2 mg/day dose of Olumiant® is safer or more effective than the other currently available, more cost-effective medications.

Recommendation:

- Add Olumiant® (baricitinib) tablets with Quantity limit = 1 tablet/day and Maximum 30 days supply to non-preferred.
  - Clinical criteria:

- Add **Olumiant additional criteria:** The patient must be ≥ 18 years of age AND The prescriber must provide a clinically valid reason why Humira, Enbrel, and Xeljanz cannot be used.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

g) Osmolex® ER (amantadine extended-release)

Amantadine, the active ingredient of Osmolex® ER, is a weak uncompetitive antagonist of the NMDA receptor. Amantadine may have direct and indirect effects on dopamine neurons and it exhibits anticholinergic-like side effects. The exact mechanism by which it works is not known. It is indicated for the treatment of Parkinson's disease and for the treatment of drug-induced extrapyramidal reactions in adult patients. Osmolex® ER tablets consist of an immediate-release outer layer and an extended-release core. The efficacy of Osmolex® ER is based upon bioavailability studies comparing Osmolex® ER to immediate-release amantadine.

Recommendation:

- Add Osmolex® ER (amantadine extended-release) QL = 1 tablet/strength/day to non-preferred.
  - Clinical criteria:
    - Add **Osmolex ER:** the patient has a documented side effect, allergy, or treatment failure with immediate release amantadine.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

h) Palynziq® (pegvaliase-pqpz)

Pegvaliase-pqpz, the active ingredient of Palynziq®, is a phenylalanine-metabolizing enzyme that is composed of recombinant phenylalanine ammonia lyase (rAvPAL) conjugated to N-hydroxysuccinimide (NHS)-methoxypolyethylene glycol (PEG). It is a PEGylated phenylalanine ammonia lyase (PAL) enzyme that converts phenylalanine to ammonia and *trans*-cinnamic acid. It substitutes for the deficient phenylalanine hydroxylase (PAH) enzyme activity in patients with phenylketonuria (PKU) and reduces blood phenylalanine concentrations. Treatment of adults with PKU resulted in the reduction of blood phenylalanine concentrations from pre-treatment baseline. It is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management. Palynziq® has a box warning regarding the increased

risk of anaphylaxis, which has been reported after use and may occur at any time during treatment. The initial dose must be administered under the supervision of a healthcare provider equipped to manage anaphylaxis, and closely watch the patient for at least 60 minutes after injection. Consider having an adult observer for patients who may need assistance in recognizing and managing anaphylaxis during treatment. *Study 301* was an open-label, randomized, multicenter study that included adults with PKU to assess the safety and tolerability of self-administered Palynziq® in an induction/titration/maintenance regimen with a target maintenance dose of 20mg SC QD or 40mg SC QD. Study 302 was an efficacy trial that included 152 patients from Study 301 and 12 patients from other Palynziq® clinical trials. Patients enrolled in Study 302 continued treatment with Palynziq® in Study 302 for up to 13 weeks to assess eligibility for randomized withdrawal period.

Recommendation:

- Add Palynziq™ (pegvaliase-pqpz) to non-preferred.
  - Clinical criteria:
    - Add **Palynziq:** Patient is 18 years of age or older AND has a diagnosis of phenylketonuria AND has uncontrolled blood phenylalanine (PHE) concentrations (> 600 micromol/L) on existing management, including restricting dietary phenylalanine and protein intake and treatment with sapropterin. For re-approval, the patient must have achieved at least a 20% reduction in PHE concentration from pre-treatment baseline or a PHE ≤ 600 micromol/L after 16 weeks of continuous treatment with the maximum dosage of 40mg daily. Note: Palynziq has a black box warning for anaphylaxis which can occur at any time during treatment. Patients, pharmacies, and physicians must be enrolled in the Palynziq REMS program AND concurrent auto-injectable epinephrine must be prescribed.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation with the addition of Kuvan® (sapropterin) to the preferred side of the PDL.

i) Roxybond® (oxycodone)

Oxycodone, the active ingredient of Roxybond®, is a full opioid agonist and is relatively selective for the mu-opioid receptor, although it can bind to other opioid receptors at higher doses. The main therapeutic action of oxycodone is analgesia. Like all full opioid agonists, there is no ceiling effect for analgesia with oxycodone. The precise mechanism of action is not known; however, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and are thought to play a role in the analgesic effects of this drug. It is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of

the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Roxybond® for use in patients for whom alternative treatment options (e.g. non-opioid analgesics or opioid combination products) have not been tolerated or are not expected to be tolerated, as well as have not provided adequate analgesia or are not expected to provide adequate analgesia. Roxybond® has a box warning regarding the increased risk of addiction, abuse, and misuse; risk evaluation and mitigation strategy (REMS); life-threatening respiratory depression; accidental ingestion; neonatal opioid withdrawal syndrome; CYP3A4 interaction; and risks from concomitant use with benzodiazepines or other CNS depressants. To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the FDA has required a REMS for these products. A clinical abuse potential study was performed, which was a randomized, double-blind, double-dummy, placebo-controlled, single-dose crossover study that included non-dependent recreational opioid users with a history of intranasal drug abuse.

Recommendation:

- Add Roxybond™ (oxycodone) to non-preferred.
  - Clinical criteria
    - Roxybond will fit into current criteria for Other Short-acting Opioids: member has had a documented side effect, allergy, or treatment failure to at least 2 medications not requiring prior approval. (If a product has an AB rated generic, one trial must be the generic)

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation with the change that for non-preferred short-acting opioids a trial of at least three other preferred short-acting medications are required.

8. New Therapeutic Drug Classes:

- None at this time

9. Therapeutic Drug Classes- Periodic Review: Jeffrey Barkin, MD and Laurie Brady, RPh, Change Healthcare

a) Leukotriene Modifiers

- No new drugs
- No new significant clinical changes

Recommendation:

- Add Zileuton ER (compare to Zyflo CR®) with Quantity Limit = 4 tablets/day to non-preferred.

- Clinical criteria
    - Revise **Montelukast:** Clinical rationale must be provided for prescribing a dose and formulation that differs from age recommendations AND If the request is for brand Singulair, the patient has a documented intolerance to the generic equivalent montelukast preparation.
    - Add Zileuton ER to the Zyflo and Zyflo CR criteria with the addition of AND if the request is for zileuton ER, the patient must have a documented intolerance to brand Zyflo CR.
    - Remove the Montelukast chewable and granules criteria.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation. After review of dosing on the Zyflo, Zyflo CR and Zileuton the quantity limit should be 4 tablets per day for all 3 agents.

b) Bronchodilators & COPD Agents

- No new drugs
- 2018 GOLD Guidelines were reviewed. Recommendations for escalation or de-escalation of treatment are now based on symptom burden and exacerbations, not degree of airflow obstruction.
    - Group A: A trial of short-acting bronchodilator for intermittent symptoms and long-acting bronchodilator for low-grade persistent symptoms is recommended with provision for stopping or switching medications on the basis of response.
    - Group B: Long-acting bronchodilator monotherapy is recommended with escalation to dual bronchodilator therapy for persistent symptoms.
    - Group C: For “frequent exacerbators” with lower symptom burden, recommendations are for use of LAMA as preferred monotherapy. For escalation of treatment, preference is given to a LAMA/LABA combination over a LABA/ICS combination based on results of one study that showed increased efficacy as well as raised concern regarding an increased risk of pneumonia associated with ICS. That may now be challenged by results of a recently published larger study showing a lower rate of moderate or severe exacerbations with LABA/ICS than with LABA/LAMA.
    - Group D: For patients with a high symptom burden and frequent or severe exacerbations, baseline therapy may include a LAMA, LABA/LAMA, or LABA/ICS with escalation to triple therapy with LABA/LAMA/ICS or addition of roflumilast or macrolide based on indications.

- For COPD short acting bronchodilators are only recommended in low risk, few symptom patients.

Recommendation:

- Add Sub-categories SHORT-ACTING BRONCHODILATORS, LONG-ACTING BRONCHODILATORS (LAMA) and COMBINATION LONG-ACTING BRONCHODILATORS (LAMA & LABA) under the preferred side of the PDL.
  - Clinical criteria
    - Remove the combined criteria of Combivent Respimat/Stiolto Respimat/Utibron Neohaler.
    - Add **Combivent Respimat:** clinical justification must be provided detailing why the patient cannot use a combination of Atrovent HFA and the preferred albuterol formulation. **Note:** Per 2018 GOLD Guidelines, Long-acting bronchodilator use is recommended for Groups B-D.
    - Revise **Spiriva Respimat:** patient has a diagnosis of COPD and a compelling clinical reason why they cannot use Spiriva Handihaler OR patient has a diagnosis of asthma and has a side effect, allergy, or treatment failure despite maximized dose of a preferred ICS/LABA combination product.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

c) Bronchodilators: Beta Agonists

- No new drugs
- No new significant clinical changes

Recommendation:

- Move PROAIR® RESPICLICK (albuterol) to preferred.
- Add Levalbuterol Aerosol (compare to Xopenex ® HFA) to non-preferred.
  - Clinical criteria
    - Remove ProAir® Respiclick from criteria.
    - Revise the criteria for **Levalbuterol (aerosol), Ventolin HFA, Xopenex HFA:** patient has a documented side effect, allergy, or treatment failure to BOTH two preferred short acting metered dose inhalers AND for approval of levalbuterol aerosol, the patient must have a documented intolerance to brand Xopenex HFA.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

d) Glucocorticoids, Inhaled

- No new drugs
- No new significant clinical changes

Recommendation:

- No changes.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

e) Sublingual Allergen Extract Immunotherapy

- No new drugs. Use of these medications was far lower than states initially expected.
- No new significant clinical changes

Recommendation:

- Remove-Grastek® (QL = 1 tablet/day) Ragwitek® from the PDL. Merck transferred rights for these medications to Alk-Abello, and they are no longer rebateable.
  - Clinical criteria
    - Remove all reference to Grastek and Ragwitek from criteria.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

10. Newly Developed/Revised Criteria:

- SGLT2 Inhibitors
- On October 30, FDA expanded Invokana's label to include reduction of MI, stroke or CV death (the composite endpoints of MACE - Major Adverse Cardiovascular Events). This was based on results of the CANVAS trial, which showed that Invokana reduced the risk of MACE by 14%, coincidentally the same reduction seen with Jardiance in the EMPA-REG trial.
  - Move INVOKANA® (canagliflozin) with Quantity limit = 1 tablet/day to preferred.
    - Clinical criteria

- Revise **Steglatro additional criteria**: Patient has a documented side effect, allergy, or contraindication to two preferred SGLT2 inhibitors.
- Revise **Invokamet, Invokamet XR, Segluromet, Synjardy, Synjardy XR, Xigduo:** Patient has documentation of a failure of therapy with a preferred SGLT2 inhibitor used in combination with metformin/metformin XR.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

11. General Announcements:
Selected FDA Safety Alerts

FDA Revises Certain Antiretroviral Drug Labeling to Not Recommend Cobicistat During Pregnancy
http://app.info.fda.gov/e/es?s=2027422842&e=159344&elqTrackId=78D8A052C380BCBFF284D754BEBE9730&elq=efcbe8abe9054ba2ad3697bb9d49fc39&elqaid=5817&elqat=1

Public Comment: No public comment.

Board Decision: No action is needed.

12. Adjourn: Meeting adjourned at 8:25 p.m.