Department of Vermont Health Access

Pharmacy Benefit Management Program

DUR Board Meeting Minutes

April 2, 2019

Board Members:

Present:

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

Absent:

Staff:

Nancy Hogue, PharmD, DVHA
Laurie Brady, RPh, Change HealthCare
Carrie Germaine, DVHA
Jennifer Egelhof, DVHA
David Aboelezz, PharmD, Change Healthcare
Laureen Biczak, DO Change Healthcare
Lisa Hurteau, PharmD, DVHA
Mike Ouellette, RPh, Change Healthcare

Guests:

Bill Eicholzier
Linda Burns, Abbott
Steven Miller, Greenwich Biosciences
Alex Felizendo, Otsuka
Karen Wachs, Greenwich Biosciences
Jeffrey Olsen, Gilead
Lisa Libera, Teva
Elizabeth Lubelczyk, Eli Lilly
Dan Michno, Lilly
Jessica Kritman, Amgen
Terry Howes, Greenwich Biosciences
Ching Lum, Alexion
Paul Isikwe, Teva
Terry Howes, Greenwich Biosciences
Paul Short, Vertex

1. Executive Session:

- An executive session was held from 6:00 p.m. until 6:35 p.m.

2. Introductions and Approval of DUR Board Minutes:

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

3. DVHA Pharmacy Administration Updates: Nancy Hogue, PharmD DVHA

- Update to S43: Medicaid was excluded from this due to having many drugs for MAT available without a PA. In lieu of excluding all PAs, a report will be required showing processing time of PAs, number of approvals and denials, Etc.

4. Medical Director Update:

- No update at this time.

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

- None at this time.

6. RetroDUR/DUR: Laurie Brady, RPh, Change Healthcare, Laureen Biczak, DO, Change Healthcare

- **Introduce: Adherence to Anti-retroviral Therapy for HIV**

The use of antiretroviral therapy has changed HIV infection from a lethal diagnosis to a chronic condition. Since the discovery of the virus, scientific advancement in understanding viral components and mechanisms of infection has led the way to increasingly effective treatment. From single therapy AZT to now triple drug therapy, improvements in survival have been nothing short of miraculous. However, drug side effects remain a significant problem and are a barrier to compliance with therapy. Unfortunately, missing only a few doses can open the door for the development of drug resistance and studies suggest that adherence rates of at least 90-95% are required for optimal viral suppression. Given that HIV infected patients often have other health issues, including substance abuse and mental health diagnoses, that challenge compliance and given the expensive nature of the antiretroviral therapies, it is worth investigating medication compliance with the goal of working with providers to improve adherence in patients.

Change Healthcare will use paid, non-reversed Medicaid pharmacy claims from calendar year 2018, excluding members with Part D and Healthy Vermonters coverage. They will evaluate only those members with continuous eligibility. Change Healthcare will identify members with at least one prescription for an anti-retroviral medication in 2018 and follow those members forward until the end of 2018 to evaluate how many were compliant with therapy using Proportion of Days Covered (PDC) methodology. The formula is similar to the Medication Possession Ratio (MPR) but instead of simply adding the days supply in a given period, the PDC considers the days that are "covered".

PDC is better suited for medication regimens consisting of multiple medications, such as antiretroviral therapy for HIV. PDC is not simply an average. Instead, it considers the days within a particular period when a patient is covered for all medications in a regimen. In other words, for a 3-drug regimen, a day is only considered "covered" when all 3 medications are available to the patient.

Use of antiretrovirals for pre-exposure prophylaxis (PrEP) are not the target of this intervention. Therefore, members on either Truvada® or Descovy® in the absence of another HIV medication in their profile will be excluded from this analysis.

Recommendation: None at this time.

Public Comment: No public comment.

Board Decision: None needed.

- **Data presentation: Sildenafil Use in Patients without a PAH diagnosis**

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 times 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 used paid, non-reversed Medicaid pharmacy claims from calendar year 2016 and compared them with claims from calendar year 2017, which is when sildenafil became a preferred drug. The goal of this analysis was to determine whether there is compliance in the treatment of PAH or if there is possible misuse for the non-covered condition of erectile dysfunction.

	Member Count	Percent of Total
Members with at least one prescription for sildenafil	245	100%
Members with at least one prescription for sildenafil BEFORE it was preferred	11	100%
Members with at least one prescription for sildenafil AFTER it was preferred	242	100%
Members with at least one prescription for sildenafil and PAH Diagnosis	13	5%
Members with at least one prescription for Sildenafil and PAH Diagnosis BEFORE Sildenafil was preferred	8	73%
Members with at least one prescription for Sildenafil and PAH Diagnosis AFTER Sildenafil was preferred	12	5%
Members with at least one prescription for sildenafil and ED Diagnosis	145	59%
Members with at least one prescription for sildenafil and ED Diagnosis BEFORE Sildenafil was preferred	1	9%
Members with at least one prescription for sildenafil and ED Diagnosis AFTER Sildenafil was preferred	144	60%
Members with at least one prescription for sildenafil with both ED and PAH Diagnosis	0	0%
Members with at least one prescription for sildenafil that didn't have either an ED or PAH Diagnosis	87	36%
Members with at least one prescription for sildenafil that didn't have either an ED or PAH Diagnosis BEFORE Sildenafil was preferred	2	18%
Members with at least one prescription for sildenafil that didn't have either an ED or PAH Diagnosis AFTER Sildenafil was preferred	86	36%

8 out of 11 patients who got sildenafil before it was preferred had a diagnosis of PAH, compared with 12 out of 242 who were prescribed sildenafil after it was preferred. Only 1 out of 11 who received sildenafil before it was preferred had a diagnosis of erectile dysfunction, compared with 144 out of242 patients after it was preferred. No members had both diagnoses.

Recommendation: After it became preferred due to low cost, there was a dramatic increase in the use of sildenafil, in doses and frequency not used for PAH. Often members were prescribed the dosage for PAH, but were prescribed daily, rather than the TID schedule used for PAH. This suggests that it is being used to treat ED, which Medicaid policy does not cover. Recommendation is that sildenafil is changed to a non-preferred drug and a prior authorization done to ensure the correct diagnosis, dosage and frequency.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

7. Clinical Update: Drug Reviews: Laureen Biczak, DO and Laurie Brady RPh, Change Healthcare

Abbreviated New Drug Reviews:

- None at this time.

Full New Drug Reviews:

a) Altreno® (tretinoin)

Tretinoin, the active ingredient of Altreno®, is a metabolite of vitamin A that binds with high affinity to specific retinoic acid receptors located in both the cytosol and nucleus. Tretinoin activates 3 members of the retinoic acid nuclear

receptors, which act to modify gene expression, subsequent protein synthesis, and epithelial cell growth and differentiation. It has not been established if the clinical effects of tretinoin are mediated through activation of retinoic receptors, other mechanisms, or both. While the exact mechanism of action in acne treatment is not known, evidence suggests that it decreases cohesiveness of follicular epithelial cells with decreased microcomedone formation. Also, tretinoin stimulates mitotic activity and increased turnover of follicular epithelial cells causing extrusion of the comedones. It is indicated for the treatment of acne vulgaris in patients 9 years of age and older. The safety and efficacy of Altreno® for the treatment of acne were assessed in 2 multicenter, randomized, double-blind studies that included subjects 9 years of age and older with acne vulgaris who had a score of moderate (3) or severe (4) on the Evaluator's Global Severity Score (EGSS), 20 to 40 inflammatory lesions (papules, pustules, and nodules), 20 to 100 non-inflammatory lesions (open and closed comedones), and 2 or fewer facial nodules. The co-primary endpoints of success on the EGSS, absolute change in non-inflammatory lesion count, and absolute change in inflammatory lesion count were assessed at week 12. Success on the EGSS was defined as at least a 2-grade improvement from baseline and an EGSS score of clear (0) or almost clear (1). It was found to be more effective as compared with vehicle for endpoints including EGSS success, non-inflammatory facial lesions and inflammatory facial lesions. While tretinoin products, brands and generics, have been available for numerous years, this is the first formulation of tretinoin in a lotion.

Recommendation:

- Defer until the review on Plixda.

Public Comment: None at this time.

Board Decision: None at this time.

b) Plixda® (adapalene)

Adapalene, the active ingredient of Plixda®, is a retinoid-like compound, and studies have shown that it is a modulator of cellular differentiation, keratinization, and inflammatory processes, all of which are important features in the pathology of acne vulgaris. Adapalene binds to specific retinoic acid nuclear receptors. While the exact mechanism of action is not known, it is thought that topical adapalene may normalize the differentiation of follicular epithelial cells resulting in decreased micocomedone formation. Plixda is an adapalene solution, 0.1%, that is available in a unit of use swab formulation. It is indicated for the topical treatment of acne vulgaris in patients 12 years of age and older. There were no clinical trials listed in the prescribing information for Plixda®. Various adapalene dosage forms, both brand and generics as well as in

combination products, have been available for numerous years and have proven safety and efficacy for treatment of acne.

Recommendation:

- Add Altreno™ and Plixda® (adapalene) 0.1% swabs to non-preferred.
- Move Differin® (adapalene) 0.1% C, G, L; 0.3% G to preferred and remove clinical criteria.
- Move TRETINOIN (specific criteria required for ages <10 or >34) 0.025%, 0.05%, 0.1% C; 0.01%, 0.025% G to non-preferred.
- Move Retin- A (tretinoin) cream and gel to preferred, noting that the microsphere formulation of both brand and generic would continue to be non-preferred.
- Remove Avage® (tazarotene), Renova® (tretinoin), Solage® (tretinoin/mequinol) and Tri-Luma® (tretinoin/hydroquinone/fluocinolone) from the PDL
    - Clinical criteria:
        - Adapalene: patient has had a documented side effect, allergy, or treatment failure with brand Differin.
        - Plixda: patient has had a documented side effect, allergy, or treatment failure with brand Differin AND a generic adapalene product.
        - Altreno, Tretinoin 0.025%, 0.05%. 0.1% C; 0.01%, 0.025% G: The diagnosis or indication is acne vulgaris, actinic keratosis or rosacea AND patient has had a documented side effect, allergy or treatment failure with a preferred tretinoin product (Avita® or Retin-A®)

Public Comments: None at this time.

Board Decision: The Board unanimously approved the above recommendation.

c) Arikayce® (amino glycosides)

Amikacin sulfate, the active ingredient of Arikayce®, is an aminoglycoside antibacterial. It is a polycationic, semisynthetic bactericidal aminoglycoside that enters the bacterial cell by binding to negatively charged components of the bacterial cell wall, disrupting the overall architecture of the cell wall. The main mechanism of action is the disruption and inhibition of protein synthesis in the target bacteria by binding to the 30S ribosomal subunit. The mechanism of resistance to amikacin in mycobacteria has been linked to mutations in the rrs gene of the 16S rRNA. In clinical trials, *Mycobacterium avium* complex (MAC) isolates developing an amikacin MIC of >64mcg/ml after baseline were observed in a higher proportion of subjects treated with Arikayce®. It is indicated in adults

who have limited or no alternative treatment options, for the treatment of *Mycobacterium avium* complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. As only limited clinical safety and effectiveness data for Arikayce® are currently available, reserve Arikayce® for use in adults who have limited or no alternative treatment options. This drug is indicated for use in a limited and specific population of patients. This indication is approved under accelerated approval based on achieving sputum culture conversion (defined as 3 consecutive negative monthly sputum cultures) by month 6. Clinical benefit has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Arikayce® has only been studied in patients with refractory MAC lung disease defined as patients who did not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. The use of Arikayce® is not recommended for patients with non-refractory MAC lung disease.. Arikayce® is for oral inhalation use only and is to be administered by nebulization only with the Lamira® Nebulizer System. Arikayce® has a box warning regarding the increased risk of respiratory adverse reactions. The safety and efficacy of Arikayce® were assessed in an open-label, randomized, multicenter study that included adults with refractory *Mycobacterium avium complex* (MAC) lung disease as confirmed by at least 2 sputum culture results. A statistically significantly larger number of patients in the Arikayce® plus background regimen group achieved culture conversion(3 consecutive monthly negative sputum cultures) by month 6 as compared with background regimen alone. Additional endpoints to assess clinical benefit, such as change from baseline in 6-minute walk test and the St. George's Respiratory Questionnaire, did not demonstrate clinical benefit by month 6.

Recommendation:

- Add Arikayce® (amikacin inhalation suspension) with (Qty limit = 28 vials (235.2 mL)/28 days) to non-preferred.
    - Clinical criteria
        - Add Arikayce: Patient is ≥ 18 years of age AND indication for use is treatment of *Mycobacterium avium complex* (MAC) lung disease AND patient has not achieved negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy (e.g. macrolide, rifampin, &

ethambutol) within the past 12 months. **Note:** Initial approval will be granted for 6 months. For re-approval, the patient must have documentation of clinical improvement AND 3 consecutive monthly negative sputum cultures.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

d) Epidiolex® (cannabidiol)

Cannabidiol, the active ingredient of Epidiolex®, is a cannabinoid that naturally occurs in the *Cannabis sativa* L. plant. While the exact mechanism of action by which it exerts its anticonvulsant effect in humans is not known, cannabidiol does not appear to exert its anticonvulsant effects through interaction with cannabinoid receptors.
Epidiolex® is a Schedule V controlled substance. It is indicated for treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS) in patients 2 years of age and older. It is recommended to obtain serum transaminases (ALT and AST) and total bilirubin levels in patients prior to the initiation of therapy, due to the risk of hepatocellular injury. The efficacy of Epidiolex® for the treatment of seizures associated with LGS was established in 2 randomized, double-blind, placebo-controlled trials that included patients aged 2 to 55 years with a diagnosis of LGS and who were inadequately controlled on at least one AED, with or without vagal nerve stimulation and/or ketogenic diet. The efficacy of Epidiolex® for treatment-resistant Dravet Syndrome (DS) was assessed in a randomized double-blind, placebo controlled study that included patients 2 to 18 years of age inadequately controlled with at least one concomitant AED, with or without vagal nerve stimulation or ketogenic diet. Compared with placebo, Epidiolex® was found to significantly reduce the frequency of drop-seizures in patients with Lennox-Gastaut Syndrome and significantly reduced the frequency of convulsive seizures in patients with Dravet syndrome. Epidiolex® was studied only against placebo. There is no evidence at this time that it is safer or more effective than other drugs used for the treatment of seizures.

Recommendation:

- Add Clobazam (compare to Onfi®) with Qty Limit = 3 tabs/day (10 mg), 2 tabs/day (20 mg)) and Epidiolex® (cannabidiol) oral solution with (Qty Limit = 20mg/kg/day) to non-preferred.
    - Clinical criteria:
        - Add Epidiolex: *Diagnosis or indication is treatment of Lennox-Gastaut Syndrome*: Serum transaminases (AST and ALT) and total bilirubin levels have been obtained prior to starting

therapy and are monitored periodically thereafter AND patient has had a documented side effect, allergy, treatment failure/inadequate response or a contraindication to at least TWO preferred anticonvulsants used for the treatment of Lennox-Gastaut syndrome AND either rufinamide or clobazam. *Diagnosis or indication is treatment of Dravet Syndrome*: serum transaminases (AST and ALT) and total bilirubin levels have been obtained prior to starting therapy and are monitored periodically thereafter AND patient has had a documented side effect, allergy, treatment failure/inadequate response or a contraindication to at least one preferred anticonvulsant and clobazam.

- Revise Clobazam, Onfi**:** diagnosis or indication is adjunctive treatment of refractory epilepsy (may include different types of epilepsy) AND patient has had a documented side effect, allergy, treatment failure/inadequate response or a contraindication to at least TWO preferred anticonvulsants AND For approval of Onfi, the patient must have documented intolerance to the generic product.

Public Comment: Steven Miller from Greenwich BioSciences: Highlighted the attributes of Epidiolex.

Board Decision: The Board unanimously approved the above recommendation.

e) Galafold® (migalastat)

Migalastat, the active ingredient of Galafold®, is an alpha-galactosidase A (alpha-Gal A) pharmacological chaperone that reversibly binds to the active site of the alpha-GAL A protein (encoded by the galactosidase alpha gene, GLA), which is deficient in Fabry disease. This binding stabilizes alpha-Gal A, allowing its trafficking from the endoplasmic reticulum into the lysosome, where it exerts its action. In the lysosome, at a lower pH and at a higher concentration of relevant substrates, migalastat dissociates from alpha-Gal A, allowing it to break down the glycosphingolipids globotriaosylceramide (GL-3) and globotriaosylsphingosine (lyso-Gb-3). Certain GLA variants, or mutations, causing Fabry disease result in the production of abnormally folded and less stable forms of the alpha-Gal A protein which retain enzymatic activity. Those GLA variants, referred to as amenable variants, produce alpha-Gal A proteins that may be stabilized by migalastat, thus restoring their trafficking to lysosomes and their intralysosomal activity. It is indicated for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase

alpha gene (GLA) variant based on in vitro assay data. This indication is approved under accelerated approval based on reduction in kidney interstitial capillary cell globotriaosylceramide (KIC GL-3) substrate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The safety and efficacy of Galafold® were assessed in a 6-month randomized, double-blind, placebo-controlled, phase followed by a 6-month open-label treatment phase and a 12-month open-label extension phase. The study included patients with Fabry disease (N=67) who were naïve to Galafold® and enzyme replacement therapy (ERT) or were previously treated with ERT and had been off ERT for at least 6 months. These patients were randomized to Galafold® or placebo during the first 6 months of the study. In the second 6 months of the study, all patients received Galafold®. The primary efficacy endpoint was the average number of GL-3 inclusions per kidney interstitial capillary (KIC) in renal biopsy samples before and after treatment. In this study, patients with non-amenable GLA variants(N=17) had no change from baseline in the number of GL-3 inclusions per KIC after 6 months of treatment..

Recommendation:

- Add FABRAZYME (agalsidase beta) IV to preferred after clinical criteria are met.
- Add Galafold™ (migalastat) with (Qty Limit = 14 caps/28 days and Maximum days' supply = 28 days) to non-preferred.
    - Clinical criteria
        - Fabrazyme: Diagnosis or indication is Fabry Disease.
        - Galafold: Patient is ≥ 18 years of age AND Diagnosis or indication is Fabry Disease with an amenable galactosidase alpha (GLA) gene variant for treatment (results must be submitted) AND enzyme replacement therapy is not a therapeutic option (e.g. due to allergy, hypersensitivity, or poor venous access).

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

f) Ilumya® (tildrakizumab-asmn)

Tildrakizumab-asmn, the active ingredient of Ilumya®, is a humanized IgG1/k monoclonal antibody that selectively binds to the p19 subunit of interleukin-23 (IL-23) and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Tildrakizumab inhibits the release of proinflammatory cytokines and chemokines. It is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are

candidates for systemic therapy or phototherapy. In 2 multicenter, randomized, double-blind, placebo-controlled trials, patients were treated with Ilumya® 100mg (N=616) or placebo (N=310) for up to 64 weeks to assess the efficacy of Ilumya® in adults with plaque psoriasis. The co-primary endpoints were the change from baseline to week 12 in PASI 75 (the proportion of subjects who achieved at least a 75% reduction in the PASI composite score) and PGA score of 0 [cleared] or 1 [minimal] (proportion of subjects who achieved a PGA score of 0 or 1 and at least a 2 point improvement).In two phase 3 clinical trials, a significantly higher proportion achieved the co-primary endpoints with Ilumya® as compared with placebo. In one of the phase 3 trials, a significantly higher number in the Ilumya® 100mg group achieved PASI 75 as compared with the active comparator etanercept; however, significant differences were not seen between these active treatments in the co-primary endpoint of PGA response. There is some evidence at this time that, like other IL inhibitors, Ilumya® is more effective than etanercept for the treatment of plaque psoriasis; however, there is no direct evidence to support that Ilumya® is safer or more effective than the other IL inhibitors, including the preferred IL inhibitor, which is a more cost-effective medication.

Recommendation:

- Add Ilumya™ (tildrakizumab-asmn) with Qty Limit = 2 ml (2 syringes) for the first month then 1 ml (1 syringe)/84 days subsequentlyto non-preferred.
    - Clinical criteria:
        - Add Ilumya to the additional criteria for Remicade, Siliq, Stelara, Taltz, Tremfya.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

g) Xofluza® (baloxavir marboixl)

Baloxavir marboxil, the active ingredient of Xofluza®, is an antiviral drug with activity against influenza virus. Baloxavir marboxil is a prodrug that is converted by hydrolysis to baloxavir, the active form that exerts anti-influenza virus activity. Baloxavir inhibits the endonuclease activity of the polymerase acidic (PA) protein, an influenza virus-specific enzyme in the viral RNA polymerase complex needed for viral gene transcription, resulting in inhibition of influenza virus replication. It is indicated for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours. There were 2 randomized controlled double-blind studies in 2 different influenza seasons that assessed the safety and efficacy of Xofluza® in otherwise healthy subjects with acute uncomplicated influenza. The overall incidence of treatment-emergent amino acid substitutions associated with reduced susceptibility to baloxavir in studies 1 and 2 was 2.7% and 11%, respectively. Prescribers

should consider currently available surveillance information on influenza virus drug susceptibility patterns and treatment effects when deciding whether to use Xofluza®. In clinical trials compared with placebo, Xofluza® resulted in statistically significant shorter time to alleviation of symptoms as compared with placebo. In one trial with olseltamivir as an active comparator, there was no difference in time to alleviation of symptoms between subjects who received Xofluza® and those that received oseltamivir.

Recommendation:

- Add Xofluza™ (baloxavir marboxil) with (Qty Limit=2 tablets/30 days) to non-preferred.
    - Clinical criteria:
        - Xofluza: Patient is ≥ 12 years of age AND there is a clinical, patient-specific reason the patient cannot use a preferred agent. **Note:** A maximum of one single dose per 30 days will be approved based on the patient's body weight: 40mg (2 x 20mg tablets) for patients weighing between 40kg and 80kg or 80mg (2 x 40mg tablets) for patients weighing at least 80kg.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

h) Ztlido® (lidocaine topical)

Ztlido® is a single-layer, drug-in-adhesive topical delivery system that is comprised of an adhesive material containing 36mg of lidocaine. Lidocaine is an amide local anesthetic that blocks sodium ion channels needed for the initiation and conduction of neuronal impulses. It is indicated for relief of pain associated with post-herpetic neuralgia (PHN). Ztlido® has different bioavailability as compared to Lidoderm®. In a single-dose, crossover study in 53 volunteers, Ztlido® 1.8% topical system demonstrated equivalent exposure and peak concentration of lidocaine to Lidoderm® patch 5%. The Ztlido® 1.8% topical system contains 36mg lidocaine while the Lidoderm® 5% patch contains 700mg of lidocaine. In a clinical study, Ztlido® resulted in adhesion scores of 0 (≥90% adhered) in 87% of the subjects. However, there is currently no evidence that Ztlido® is safer or more effective than the other available cost-effective treatments for PHN.

Recommendation:

- Add Ztlido™ Patch (lidocaine 1.8%) with Qty Limit = 3 patches/day to non-preferred.
    - Clinical criteria:
        - Add Ztlido to the Qutenza revised criteria: diagnosis or indication is post-herpetic neuralgia AND patient has had a documented side effect, allergy, treatment failure or contraindication to 2 drugs in the tricyclic antidepressant (TCA) class and/or anticonvulsant class as well as Lyrica and Lidocaine patch OR patient has a medical necessity for

transdermal formulation (ex. dysphagia, inability to take oral medications) AND patient has had a documented side effect, allergy, treatment failure or contraindication to Lidocaine patch.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

8. New Therapeutic Drug Classes

- None at this time.

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

a) Anti- hypertensives: Angiotensin Modulators

- No new drugs.
- No new significant clinical changes.
- Brand name Atacand® (candesartan) and Atacand/HCT® (candesartan/HCT) are rebatable but have an obsolete date of 10/2018.

Recommendation:

Angiotensin Modulators

- Remove Mavik® (trandolapril), Atacand HCT (candesartan/hydrochlorothiazide) and Atacand® (candesartan) from the PDL and criteria.
- Move Trandolapril/Verapamil ER (compare to Tarka®), Micardis HCT® (Telmisartan/hydrochlorothiazide) and Exforge HCT® (amlodipine/valsartan/hydrochlorothiazide) (Qty limit = 1 tablet/day) to non-preferred.
- Move Olmesartan (compare to Benicar®) and Valsartan/Amlodipine/HCTZ (compare to Exforge HCT®) with Qty Limit = 1 tablet/day to preferred.
    - Clinical criteria:
        - Add Tarka and Trandolapril/Verapamil ER to the Prestalia criteria.
        - Update the criteria for Avapro, Benicar, Candasertan, Cozaar, Diovan, Edarbi, Eprosartan, and Telmisartan to say two preferred Angiotensin Receptor Blocker (ARB) or ARB combinations must be tried and failed.
        - Remove criteria for Valsartan/amlodipine, Exforge, Valsartan/amlodipine/HCTZ, Tribenzor and Exforge HCT.
        - Add Exforge HCT, Tribenzor: patient has had a documented side effect, allergy, or treatment failure to Valsartan/amlodipine/HCTZ.

        - Revise Azor, Amlodipine/Telmisartan, Exforge, Olmesartan/amlodipine, Olmesartan/amlodipine/HCTZ and Twynsta: The patient has had a documented side effect, allergy, or treatment failure to Valsartan/amlodipine.
- Renin InhibitorsAdd Aliskiren (compare to Tekturna®) with Qty Limit = 1 tablet/day to non-preferred.
    - Clinical criteria:
        - Add Aliskiren to the Tekturna criteria.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

b) Anti-hypertensives: Beta Blockers

- New authorized generic for Coreg CR®, Carvedilol CR.
- No new significant clinical changes

<u>Recommendation:</u>

Anti-hypertensive: Beta Blocker

- Add Carvedilol CR (compare to Coreg CR®) with Qty Limit = 1 tablet/day to non-preferred.
- Remove Trandate® (labetaolol), Lopressor HCT® (metoprolol/HCTZ), and Dutoprol® (metoprolol succinate XR/hydrochlorothiazide) from the PDL.
    - Clinical criteria
        - Add Carvedilol CR to the Coreg CR criteria.

Coronary Vasodilators/Antianginals/Sinus Node Inhibitors

- Remove NITREK® (nitroglycerin transdermal patch), NITROGLYCERIN ER capsule, , NITROQUICK® (nitroglycerin SL tablet), NITRO-TIME® (nitroglycerin ER capsule), Imdur® (isosorbide mononitrate ER tablet), Ismo® (isosorbide mononitrate tablet) and Monoket® (isosorbide mononitrate tablet) from the PDL and criteria.
- Add Ranolazine tablet (compare to Ranexa®) with Qty Limit = 3 tablets/day (500 mg), 2 tablets/day (1000 mg) to non-preferred.
- Move Nitrolingual Pump Spray® to non-preferred.
        - Clinical criteria:
            - Revise Dilatrate-SR, Isosorbide dinitrate SL tablet, Isordil: The patient has had a side effect, allergy, or treatment failure to at least two preferred agents.
            - Add Nitrolingual Pump Spray®: The patient has had a side effect, allergy, or treatment failure to Nitroglycerin spray lingual.
            - Add Ranolazine to the Ranexa criteria.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

c) Anti-hypertensives: Calcium Channel Blockers

- No new drugs
- No new significant clinical changes

Recommendation:

- Clarify Diltiazem ER and SR 24-hour tablets and capsules are preferred
- Move Diltiazem ER 12 hour capsules from Non-preferred Dihydropyridines to Non-preferred Miscellaneous Calcium Channel Blockers
- Remove Afeditab® CR (nifedipine SR, compare to Adalat® CC) from the PDL

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

d) Antimigraine Agents, Triptans & CGRP Antagonists (NDR Ajovy® (fremanezumab- vfrm) and NDR Emgality® (galcanezumab- gnlm) included)

- New drug Ajovy® (fremanezumab-vfrm)

Fremanezumab-vfrm, the active ingredient of Ajovy®, is a humanized IgG2Δ a/kappa monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand that is produced by recombinant DNA. It binds to CGRP ligand and blocks its binding to the receptor. It is indicated for the preventive treatment of migraine in adults. Ajovy® has 2 dosing options, 225mg SC monthly or 675mg every 3 months which is given as 3 consecutive SC injections of 225mg each. The safety and efficacy of Ajovy® were assessed in 2 multicenter, randomized, 3-month, double-blind, placebo-controlled studies. In clinical trials compared with placebo, Ajovy® significantly reduced the monthly average number of migraine days (and number of headache days of at least moderate severity), as well as improved response rates, in adults with episodic or chronic migraine. Ajovy® is the second CGRP antagonist to be approved in 2018, with a prior FDA approval of Aimovig® that carries the same indication as Ajovy®. No comparator studies with Ajovy® and other treatments for the prevention of migraine were found. Ajovy® can provide modest improvements in outcomes for patients with chronic migraine and some patients with frequent episodic migraine.. Given the lack of comparative and long-term efficacy and safety data and the high cost of the drug, Ajovy® should be non-preferred and be authorized only for patients who are unable to tolerate or who have had inadequate response to the other preferred medications used for migraine prophylaxis.

- New drug Emgality® (galcanezumab- gnlm)

Galcanezumab-gnlm, the active ingredient of Emgality®, is a humanized IgG4 monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand that is produced by

recombinant DNA technology. It binds to CGRP ligand and blocks its binding to the receptor. It is indicated for the preventive treatment of migraine in adults. Emgality® requires a loading dose of 240mg SC (2 consecutive SC injections of 120mg) followed by monthly doses of 120 mg SC. The safety and efficacy of Emgality® were assessed as preventive treatment of episodic or chronic migraine in 3 multicenter, randomized, double-blind, placebo-controlled studies that included two 6-month studies in patients with episodic migraine and one 3-month study in patients with chronic migraine. In clinical trials compared with placebo, Emgality® significantly reduced the number of monthly migraine headache days, as well as improved response rates, in adults with chronic or episodic migraines. Emgality® is the third CGRP antagonist to be approved in 2018, with a prior FDA approval of Aimovig® and Ajovy® that have the same indication as Emgality®. No comparator studies with Emgality® and other treatments for the prevention of migraine were found. Emgality® can provide modest improvements in outcomes for patients with chronic migraine and some patients with frequent episodic migraine..

Recommendation:

- Add Emgality® (galcanezumab-gnlm) withQty Limit = 240mg (2 injections) for the first 30 days followed by 120 mg (1 injection) per 30 days to preferred after clinical criteria are met.
- Add Ajovy® (fremanezumab-vfrm) with Qty Limit = 225mg (1 injection) per 30 days or 675mg (3 injections) every 90 days to non-preferred.
- Update the Qty Limit = 140mg per 30 days for Aimovig.
- Add Qty Limit= 4 injections/30 days for Zembrace SymTouch.
- Change Qty limits listed from per month to per 30 days for clarification purposes.
- Remove Alsuma® (sumatriptan) from the PDL.
    - Clinical criteria:
        - Existing Aimovig criteria will be revised to state all agents.
        - Add Aimovig, Ajovy additional criteria: The patient must have a documented side effect, allergy, or treatment failure to Emgality.

Public Comment: Elizabeth Lubelczyk from Eli Lilly: Highlighted the attributes of Emgality.
Paul Isikwe from Teva: Highlighted the attributes of Ajovy.

Board Decision: The Board unanimously approved the above recommendation.

e) Biles Salts

- No new drugs.
- No new significant clinical changes.

Recommendation:

- No changes at this time.

Public Comment: No public comment.

Board Decision: None needed.

f) Botulinum Toxin

- No new drugs.
- The Canadian Urological Association (CUA) published guidelines for the treatment of adult overactive bladder (OAB) in 2017.
- In 2018, the European Headache Federation published a guideline on the use of OnabotulinumtoxinA (ONA) in chronic migraine. The expert group recommends ONA as an effective (Level B) and well-tolerated (Level A) treatment of chronic migraine. Patients eligible for ONA should have tried 2-3 other migraine prophylactics before starting ONA. ONA should be administered according to the PREEMPT injection protocol every 12 weeks. Patients are defined as non-responders if they have less than 30% reduction in headache days per month during treatment with ONA and treatment should be discontinued if the patient does not respond to the first 2-3 treatment cycles.
- In 2018, Arruda et al99 performed a systematic review and meta-analysis of 7 prospective, randomized, placebo-controlled clinical trials evaluating the treatment of non-neurogenic overactive bladder with ONA. For all primary endpoints, the toxin was more effective than placebo ($p<0.0001$) namely: urgency (mean difference= -2.07), voiding frequency (mean difference= -1.64), nocturia (mean difference= -0.25) and incontinence episodes (mean difference= -2.06). The need for intermittent catheterization and the occurrence of urinary tract infection (UTI) were more frequent in patients treated with ONA than in the placebo group ($p<0.0001$). The analysis concluded that compared to placebo, ONA had significantly and clinically relevant reductions in OAB symptoms but is associated with higher incidence of intermittent catheterization and UTI.
- In 2018, Fu et al103 completed a systematic review and network meta-analysis evaluating different therapies for treating spasticity associated with multiple sclerosis. Percentages of improved patient spasticity scale, mild adverse effects, and severe adverse effects were extracted as outcomes. There were 23 randomized controlled trials (N=2720) included. Cannabinoids and botulinum toxin both showed significantly greater efficacy than placebo in the percentage of improved patients' spasticity (OR 1.92 for cannabinoids and OR 16.44 for botulinum toxin). Botulinum toxin showed significantly greater efficacy compared with tizanidine (OR 15.49) and baclofen (OR 15.18). No further significant differences were observed in other comparisons of improved patients. No significant difference was found in spasticity scales (Ashworth Scale or modified Ashworth Scale). Cannabinoids, diazepam, and tizanidine had significantly more mild adverse effects than placebo. The authors recommend botulinum toxin as the optimal intervention for multiple sclerosis-related spasticity. Cannabinoids

and transcutaneous electric nerve stimulation could also be considered as treatments but their safety remained to be verified.
- Xeomin (incobotulinumtoxinA) received approval for the indication of chronic sialorrhea.

Recommendation:

- Update the chronic migraine definition in Botox criteria ≥ 15 headache days per month, of which ≥ 8 are migraine days.
- Update Xeomin criteria:The patient is ≥ 18 years of age AND the patient has a diagnosis of cervical dystonia, upper limb spasticity, or blepharospasm OR the patient has a diagnosis of chronic sialorrhea and has a documented side effect, allergy, treatment failure, or contraindication to at least two anticholinergic agents (e.g. scopolamine, glycopyrrolate).

Public Comment: from: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

g) Lipotropics: Statins

- No new drugs.
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- In 2018, Grundy et al[222] published a report of the American College of Cardiology/American Heart Association Task Force on Clinical practice guidelines on the management of blood cholesterol.

Recommendation:

- Remove Mevacor® (lovastatin) from the PDL.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

h) Lipotropics: Other

- New generic for Welchol®, Colesevelam tablets
- Kynamro ® (Mipomersen sodium) , FDA approved in 2013, has been discontinued by the manufacturer.
- A 2018 Cochrane Review by Abdelhamid et al[216] included 49 randomized controlled trials (N=24,272) to assess the effects of increasing total polyunsaturated fatty acid (PUFA) intake on cardiovascular disease and all-cause mortality and lipids in adults. Results suggested that increasing PUFA intake probably has little or no effect on all-cause mortality (risk 7.8% vs

7.6%, risk ratio [RR] 0.98, 24 studies) but probably slightly reduces the risk of coronary heart disease events.

- In 2018, Grundy et al[222] published a report of the American College of Cardiology/American Heart Association Task Force on Clinical practice guidelines on the management of blood cholesterol. These updated guidelines incorporate use of ezetimibe and PCSK9 Inhibitors.

Recommendation:

- Add Colesevelam (compare to Welchol®) to non-preferred.
- Move Ezetimibe (compare to Zetia®) with Qty Limit = 1 tablet/day to preferred.
- Move Zetia® (ezetimibe) with Qty Limit = 1 tablet/day to non-preferred.
- Remove Lofibra® (fenofibrate micronized) Capsules 67mg, 134 mg, 200 mg, Lofibra® (fenofibrate) Tablets 54 mg, 160 mg, Kynamro® (Mipomersen) Syringe for Subcutaneous Injection NIACOR® (niacin) and Advicor® (lovastatin/extended release niacin) from the PDL.
    - Clinical criteria:
        - Add Colesevelam: The patient has had a documented intolerance to the brand name equivalent.
        - Remove Ezetimibe and Advicor criteria.
        - Add Zetia: patient must have a documented intolerance to the generic equivalent.
        - Add to Criteria for Approval for PCSK9 Inhibitors: Inability to reach goal LDL-C despite a trial of 2 or more maximum tolerated dose of statins (one of which must be atorvastatin or rosuvastatin) and ezetimibe 10mg daily. Remove this statement for the additional criteria for each diagnosis.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

10. Newly Developed/Revised Criteria:

- None at this time.

Public Comment: No public comment.

Board Decision: None at this time**.**

11. General Announcements: Michael Ouellette, RPh, Change Healthcare

Selected FDA Safety Alerts

FDA adds Boxed Warning for increased risk of death with gout medicine Uloric (febuxostat) https://www.fda.gov/Drugs/DrugSafety/ucm631182.htm

Safety trial finds risk of blood clots in the lungs and death with higher dose of tofacitinib (Xeljanz, Xeljanz XR) in rheumatoid arthritis patients; FDA to investigate https://www.fda.gov/Drugs/DrugSafety/ucm631871.htm?utm_campaign=New%20FDA%20Drug%20Safety%20Communication%20on%20tofacitinib%20-%20Drug%20Information%20Update&utm_medium=email&utm_source=Eloqua

FDA in Brief: FDA updates label for Chantix with data underscoring it's not effective in children 16 and younger https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm631875.htm?utm_campaign=FDA%20updates%20prescribing%20information%20for%20Chantix%20%28varenicline%29%20with%20data&utm_medium=email&utm_source=Eloqua

Public Comment: No public comment.

Board Decision: No action is needed.

12. Adjourn: Meeting adjourned at 8:30 p.m.