Department of Vermont Health Access
Pharmacy Benefit Management Program
DUR Board Meeting Minutes
June 21, 2022

Board Members Present:

Mark Pasanen, MD
Bill Breen, RPH
Margot Kagan, PharmD
Andy Miller, RPH
Renee Mosier, PharmD
Douglas Franzoni, PharmD

Absent: Joseph Nasca, MD, Claudia Berger, MD, Lucy Miller, MD

Staff:

Laurie Brady, RPh, Change HealthCare
Marietta Scholten, Physician Consultant, DVHA
Laureen Biczak, DO, Change Healthcare
Lisa Hurteau, PharmD, DVHA
Stacey Baker, DVHA
Carrie Germaine, DVHA

Guests: Adam Denman (Global Blood Therapeutics), Folger Tuggle (Alnylam Pharmaceuticals), Paul Amato (Viiv Healthcare), Lindsey Walter (Novartis), Taylor Robichaud, Santreis Booze (Global Blood Therapeutics), Beth D'Ambrosio (Novartis), Kristen Chopas (Gilead), Janet R., Lisa Libera (Teva Pharmaceuticals), Steven Patterson (Neurelis), Alain Nguyen (Gilead), Eric Sherr (Viiv Healthcare)

1. Executive Session:

- An executive session was held from 6:00 p.m. until 6:30 p.m.

2. Introductions and Approval of DUR Board Minutes:

- Attendance was called and introductions of DVHA and Change Healthcare staff were made.
- The May meeting minutes were accepted as printed. Margot Kagan abstained from voting.

3. DVHA Pharmacy Administration Update: Lisa Hurteau, Pharm.D., DVHA:

- The terms for Renee Mosier, PharmD and Bill Breen, RPH expire at the end of August. Lisa thanked them for their expertise and participation in the DUR Board activities. A new chair will need to be elected at the September meeting.
- DVHA is in the process of hiring a new clinical pharmacist. They are not yet able to make the official announcement but are hopeful the new employee will be present at the September meeting.

- H728, a house bill that would have impacted DUR activity related to medication assisted treatment (MAT), was vetoed by Governor Scott.

4. Medical Director Update: Marietta Scholten, Physician Consultant, DVHA

- DVHA is conducting second round interviews for a Chief Medical Officer.

6. Follow-up Items from Previous Meetings: Laurie Brady, RPH Change Healthcare

- None at this time.

7. RetroDUR/ProDUR: Laurie Brady, RPh, Change Healthcare

- Introduction: Metabolic Monitoring for Children and Adolescents on Antypsychotics

Antipsychotics, while effective in treating schizophrenia and other disorders, such as bipolar disorder, depression, anxiety, and autism, can have significant side effects. The atypical antipsychotics have fewer severe side effects than the typical antipsychotics, however metabolic effects are still a concern. Additionally, as the use of the antipsychotic medications has increased for disorders other than schizophrenia and psychosis, there is a paucity of evidence from randomized clinical trials for use in children with such disorders. Generally, because of a lack of data showing superiority of any particular antipsychotic (other than clozapine), decisions about treatment should include the side effect profiles and risks to the particular patient. Side effects from antipsychotics as a group include extrapyramidal symptoms, significant weight gain, metabolic syndrome, liver function abnormalities, QT prolongation, and bone marrow suppression, although the drugs vary in risk profiles. Prior to starting antipsychotics, patients should have baseline studies including CBC, fasting glucose, lipid profile (including triglycerides), transaminases, HbA1c and ECG with QTc. At 4 weeks a CBC should be repeated and at 12 weeks, repeat of CBC, fasting plasma glucose and lipid profiles are recommended. These labs and ECGs should all be repeated annually as well.

Change Healthcare will use paid, non-reversed Medicaid pharmacy and medical claims from SFY 2021, excluding members with Part D, TPL, VMAP and Healthy Vermonters coverage. Only members with continuous Medicaid coverage will be used in the analysis. They will identify members 18 years and younger who were started on antipsychotic medications in 2021 and evaluate if appropriate laboratory monitoring was done at baseline and 12 weeks after starting therapy. Specifically, we will look for CBC, fasting plasma glucose and lipid profile measurements.

Recommendation: None at this time.

Public Comment: No public comment.

Board Decision: Renee Mosier requested that some leniencies be given with the timeline for which labs were drawn.

- Data presentation: Concomitant use of GLP-1 agonists and DPP-4 inhibitors in Type II DM

Treatment for Type 2 Diabetes Mellitus (DM) has improved substantially in the last decade. Several effective newer classes of medications are now available, including glucagon-like peptide-1 receptor agonists (GLP-1 agonists), sodium-glucose co-transporter 2 inhibitors (SGLT-2 inhibitors) and dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors, also called gliptins), along with older medications, such as sulfonylureas and insulin. Recent guidelines from the American Diabetes Association and the American Society of Endocrinology incorporate these newer agents into treatment algorithms, often recommending considering these drugs before starting insulin therapy. Some of these agents have beneficial effects on other risks, such as heart failure and other cardiovascular diseases, and determining which drugs to use depends on an individual's health profile. GLP-1 receptor agonists work by stimulating insulin secretion and decreasing glucagon production. DPP-4 inhibitors prevent the degradation of GLP-1. Both have shown benefit in lowering blood glucose, however comparative trials have shown GLP-1 receptor agonists to be superior in improving glycemic control and inducing weight loss. Studies have shown that combining a GLP-1 agonist with a DPP-4 inhibitor provides minimal improvement in glycemic control and weight loss compared with either monotherapy, and combination therapy is not cost effective. Guidelines do not support combined therapy with these drugs.

Change Healthcare used paid, non-reversed Medicaid pharmacy claims from January 2021 – December 2021, excluding members with Part D or other insurance as primary coverage, VMAP, and Healthy Vermonters coverage. They looked at members to see if they were being prescribed both a DPP-4 inhibitor and GLP-1 receptor agonist to determine if the practice was widespread or isolated among a few providers. The following GLP-1 Receptor Agonists were included in the analysis: Adlyxin®(lixisenatide), Bydureon (exenatide extended-release), Bydureon® BCise™ (exenatide extended-release), Byetta® (exenatide), Ozempic® (semaglutide), Rybelsus® (semaglutide), Soliqua® (insulin glargine/lixisenatide), Trulicity® (dulaglutide), and Victoza® (liraglutide). The following DPP-4 Inhibitors and combinations were included in the analysis: Janumet® (sitagliptin/metformin), Janumet® XR (sitagliptin/metformin ER), Januvia® (sitagliptin), Jentadueto® (linagliptin/metformin), Jentadueto® XR (linagliptin/metformin ER), Kazano® (alogliptin/metformin), Kombiglyze® XR (saxagliptin/metformin ER), Nesina® (alogliptin), Onglyza® (saxagliptin), Oseni® (alogliptin/pioglitazone), and Tradjenta® (linagliptin).

There were 1,100 members taking only a GLP-1 RA and 281 member taking only a DPP-4 Inhibitor. 76 members had an overlapping claim with a medication from each class. 26 members had an overlap of more than 90 days, and 13 members had an overlap of more than 180 days. The most common combination of medications that overlapped were Trulicty® and Januvia®.

Recommendation: Fortunately, there were few members (76) who were concurrently taking a GLP-1 receptor agonist and DPP-4 inhibitor to treat their diabetes. This overlap in some patients may have been because of a transition from one drug to another. However, there were still a total 26 patients who were on both for more than 90 days, and 13 whose overlap exceeded 180

days. Options for education include a general educational mailing to providers who prescribe diabetic medications, but an intervention targeting the prescribers of these medications where overlap exceeds 90 or 180 days might be more effective.

Public Comment: No public comment.

Board Decision: The board unanimously agreed to send a targeted communication to the prescribers of the 13 members with claim overlap of great than 180 days.

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

Biosimilar Drug Reviews:

- None at this time.

Full New Drug Reviews:

- Apretude® (cabotegravir extended-release injectable suspension)

Cabotegravir, the active ingredient of Apretude®, is an HIV-1 integrase strand transfer inhibitor (INSTI). This inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral DNA integration that is essential for the HIV replication cycle. It is indicated in at-risk adults and adolescents weighing at least 35kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test prior to initiating Apretude® (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP. The safety and efficacy of Apretude® to reduce the risk of acquiring HIV-1 infection were assessed in 2 randomized, double-blind, controlled, multinational trials, including HPTN 083 (in HIV-1 uninfected men and transgender women who have sex with men and have evidence of high-risk behavior for HIV-1 infection) and HPTN 084 (in HIV-1 uninfected cisgender women at risk of acquiring HIV-1). In clinical trials, it was compared with oral Truvada® and the primary analysis demonstrated the superiority of Apretude® compared with Truvada® with an 88% reduction in the risk of acquiring incident HIV-1 infection (study HPTN 084) and with a 66% reduction in the risk of acquiring HIV-1 infection (study HPTN 083). Apretude® is a relatively safe, effective, and cost-effective medication. It is therefore recommended that it be preferred and available without prior authorization.

Recommendation:

- Add new sub-category of Pre-exposure Prophylaxis (PrEP). Add Apretude® (cabotegravir extended-release) 600mg/3 mL IM injection, Descovy® (emtricitabine/tenofovir AF) 200mg/25mg tablet, and Emtricitabine/Tenofovir DF (compare to Truvada®) 200mg/300mg tablet to preferred.
- Add Truvada® (Emtricitabine/Tenofovir DF) 200mg/300 mg tablet to non-preferred.
    - Clinical criteria:
        - Add Truvada: The patient has a documented intolerance to the generic equivalent.

Public Comment: Paul Amato, Pharm D (Viiv Healthcare) highlighted the attributes of Apretude®.

Board Decision: The Board unanimously approved the above recommendations.

- Livtencity® (maribavir)

Maribavir, the active ingredient of Livtencity®, is a benzimidazole riboside cytomegalovirus (CMV) pUL97 protein kinase inhibitor. It is an antiviral agent against human CMV, mediated by competitive inhibition of the protein kinase activity of human CMV enzyme pUL97, which results in inhibition of the phosphorylation of proteins. It is indicated for the treatment of adults and pediatric patients (12 years of age and older and weighing at least 35kg) with post-transplant cytomegalovirus (CMV) infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir, or foscarnet. A phase 3, multicenter, randomized, open-label, active-controlled, superiority trial was performed to assess the safety and efficacy of Livtencity® as compared to Investigator-Assigned Treatment (IAT; ganciclovir, valganciclovir, foscarnet, or cidofovir) in hematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT) recipients with CMV infections (N=352) that were refractory to treatment with ganciclovir, valganciclovir, foscarnet, or cidofovir, including CMV infections with or without confirmed resistance to 1 or more of the IATs. Subjects with CMV disease involving the CNS, including the retina, were excluded from the study. Subjects were randomized to treatment for up to 8 weeks; and, after completion of the treatment period, subjects entered a 12-week follow-up phase. The primary efficacy endpoint was confirmed CMV DNA level <LLOQ at the end of week 8, and results suggested that Livtencity® was statistically superior to IAT (56% vs 24%, respectively; NNT 4). There is some evidence at this time to suggest that Livtencity® is more effective than the other currently preferred, more cost-effective medications (ganciclovir, valganciclovir, foscarnet, or cidofovir) in a phase 3 study for the primary endpoint of confirmed CMV DNA level <LLOQ (i.e. <137IU/ml). However, there is no evidence to suggest that Livtencity® is safer than the other currently preferred medications.

Recommendation:

- Add Livtencity® (maribavir) to non-preferred.
  - Clinical criteria:
    - Add Livtencity: Indication is for the treatment of CMV infection in a recipient of a hematopoietic stem cell or solid organ transplant AND infection is refractory to ganciclovir, valganciclovir, cidofovir, or foscarnet (as defined by >1 $\log_{10}$ increase in CMV DNA levels in blood or serum after at least 14 days of therapy) AND medication will not be administered with ganciclovir or valganciclovir. For re-approval beyond 12 weeks, documentation must be submitted detailing continued medical necessity.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- Voxzogo® (vosoritide)

Vosoritide, the active ingredient of Voxzogo®, is a human C type natriuretic peptide (CNP) analog, a 39 amino acid peptide. In patients with achondroplasia, endochondral bone growth is negatively regulated due to a gain of function mutation in fibroblast growth factor receptor 3 (FGFR3). Binding of vosoritide to natriuretic peptide receptor-B (NPR-B) antagonizes FGFR3 downstream signaling by inhibiting the extracellular signal-regulated kinases 1 and 2 (ERK1/2) in the mitogen-activated protein kinase (MAPK) pathway at the level of rapidly accelerating fibrosarcoma serine/threonine protein kinase (RAF-1). As a result, vosoritide, like CNP, acts as a positive regulator of endochondral bone growth as it promotes chondrocyte proliferation and differentiation. It is indicated to increase linear growth in pediatric patients with achondroplasia who are 5 years of age and older with open epiphyses. This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). The safety and efficacy of Voxzogo® were assessed in one multicenter, randomized, double-blind, placebo-controlled study of 52 weeks in duration that included patients with genetically confirmed achondroplasia (N=121) who were randomized to either Voxzogo® or placebo. Voxzogo® treatment for 52 weeks resulted in a treatment difference in the change from baseline in AGV of 1.57 cm/year ($p<0.0001$). It is recommended that Voxzogo® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

Recommendation:

- Add new sub-category Achondroplasia Treatments with note that all products require PA.
- Add Voxzogo® (vosoritide) to non-preferred.
    - Clinical criteria:
        - Add Voxzogo: The patient must have a diagnosis of achondroplasia confirmed with genetic testing AND the medication must be prescribed by a pediatric endocrinologist AND Confirmation of non-closure of epiphyseal plates (x-ray determining bone age) must be provided for females > age 12 and males > age 14 AND Voxzogo will not be used in combination with growth hormone (e.g. somatropin), growth hormone analogs (e.g. somapacitan), or insulin-like growth factor (IGF-1) (e.g. mecasermin) AND patient's standing height, weight, BMI, and upper to lower body ratio will be measured at baseline and monitored throughout therapy. For re-approval, the patient must have an improvement in growth velocity compared to pre-treatment baseline.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- Vuity® (pilocarpine)

Pilocarpine, the active ingredient of Vuity®, is a cholinergic muscarinic receptor agonist which activates muscarinic receptors located at smooth muscles, such as the iris sphincter muscle and ciliary muscle. Vuity® contracts the iris sphincter muscle, constricting the pupil to improve near and intermediate visual acuity while maintaining some pupillary response to light. Vuity® also contracts the ciliary muscle and may shift the eye to a more myopic state. It is indicated for the treatment of presbyopia in adults. The efficacy of Vuity® for the treatment of presbyopia was demonstrated in two 30-day phase 3, randomized, double-masked, vehicle-controlled studies (GEMINI 1 and GEMINI 2). Adults aged 40 to 55 years of age with presbyopia (N=750) were randomized to Vuity® or vehicle once daily in each eye. In two vehicle-controlled studies, a significantly greater number of subjects in the Vuity® group as compared with the vehicle group gained 3 lines or more in mesopic, high contrast, binocular distance corrected near visual acuity (DCNVA), without losing more than 1 line (5 letters) of corrected distance visual acuity (CDVA) with the same refractive correction. Per an AbbVie press release, Vuity is "…an optimized formulation of pilocarpine…delivered with proprietary pHast® technology, which allows Vuity® to rapidly adjust to the physiologic pH of the tear film." Pilocarpine ophthalmic solution 1%, 2% and 4% is available from multiple generic manufacturers and is indicated for glaucoma, ocular hypertension and miosis induction.

Recommendation:

- Add new sub-category Presbyopia Agents with a note that all products require PA.
- Add Vuity™ (pilocarpine) 1.25% solution to non-preferred
  - Clinical criteria:
    - Add Vuity: The patient has a diagnosis of presbyopia AND the patient is between the ages of 40-55 at the time of therapy initiation AND the medication is being prescribed by or in consultation with an optometrist or ophthalmologist AND the patient has failed corrective eyeglasses or contact lenses, unless contraindicated

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

9. New Therapeutic Drug Classes

- None at this time.

10. Therapeutic Drug Classes- Periodic Review:

- **Anticonvulsants (new drug Eprontia® (topiramate solution) included)**
  - The mechanism by which topiramate, the active ingredient of Eprontia®, works is not known; however, preclinical studies have revealed 4 properties that may contribute to its efficacy for epilepsy and the preventive treatment of migraine. Electrophysiological and biochemical evidence suggests that topiramate, at pharmacologically relevant concentrations, blocks voltage-dependent sodium channels, augments the activity of the neurotransmitter gamma-aminobutyrate at some subtypes of the GABA-A receptor, antagonizes the AMPA/kainate subtype of the glutamate receptor, and inhibits the carbonic anhydrase enzyme, particularly isozymes II and IV. It is indicated for initial monotherapy for the treatment of partial-onset or primary generalized tonic-clonic seizures in patients 2 years of age and older, Adjunctive therapy for the treatment of partial-onset seizures, primary generalized tonic-clonic seizures, and seizures associated with Lennox-Gastaut syndrome in patients 2 years of age and older and the preventive treatment of migraine in patients 12 years and older. The safety and efficacy of Eprontia® are based on the relative bioavailability of Eprontia® compared to topiramate sprinkle capsules in healthy subjects. Topiramate sprinkle capsules have comparable bioavailability to topiramate tablets. The studies described in the prescribing information of Eprontia® were conducted using topiramate tablets or sprinkle capsules. Topiramate, under the brand name Topamax®, has been available for numerous years as both a brand and generic, with the same indications as Eprontia®. Eprontia® offers providers another treatment option with this new dosage form.
  - In 2021, Devi et al published a literature review and indirect treatment comparison of the short-term efficacy and safety of add-on anti-seizure medications in Dravet syndrome (DS). Five randomized controlled trials (RCTs) with 565 patients with DS (2–20 years) who received placebo or any of the three active interventions (stiripentol, cannabidiol, and fenfluramine) were included. The studies consisted of 565 patients with DS [mean (SD) age: 9.3 (6.0) years; 287 (51%) males] with a mean (SD) baseline monthly convulsive seizures frequency of 22.0 (94.7) seizures. Among the five included studies, stiripentol was the intervention in one study, while cannabidiol and fenfluramine were the interventions in two studies each. Among the included RCTs, 124/232 (53%) participants in the intervention group (cannabidiol: N = 59/128 (46%); fenfluramine: N = 50/83 (60%); and stiripentol: N = 15/21 (71%)) and 41/228 (18%) participants in the placebo group achieved ≥50% reduction in convulsive seizure frequency from baseline. In pairwise meta-analysis, a statistically significant number of patients with ≥50% reduction in convulsive seizure was reported with cannabidiol [OR: 2.4; 95% CI: 1.4–4.0; number of studies (nos): 2], fenfluramine [OR: 17.4; 95% CI: 6.9–43.7; nos: 2], and

stiripentol [OR: 47.5; 95% CI: 5.1–438.5; nos: 1] as compared with placebo for this outcome. However, on indirect comparison stiripentol [OR: 20.2; 95% CI: 2.05–198.0] and fenfluramine [OR: 7.4; 95% CI: 2.6–21.4] had greater odds for ≥50% reduction in convulsive seizure frequency than cannabidiol. Among the three treatments, stiripentol (0.93) had the highest probability of achieving ≥50% reduction in convulsive seizure frequency from baseline. Among the included RCTs, 24/232 (12%) participants achieved nearly 100% seizure reduction during the treatment with interventional drugs (cannabidiol: N = 6/128 (5%), fenfluramine: N = 9/83 (11%), and stiripentol: N = 9/21 (43%)) while 1/228 (0.4%) participants in the placebo arm achieved this outcome. Among the included RCTs, 220/234 (94%) patients experienced TEAEs in interventional group (cannabidiol: N = 119/130 (92%); fenfluramine: N = 80/83 (96%); and stiripentol: N = 21/21 (100%)) as compared with 175/228 (77%) in the placebo group. In pairwise meta-analysis, stiripentol was associated with a significantly greater frequency of TEAEs [OR: 121.2; 95% CI: 4.1–3544.3; nos: 1]. Further, it was associated with a significantly higher frequency of TEAEs [OR: 53.9; 95% CI: 1.4–2079.8] compared with cannabidiol. Also, stiripentol (0.97) had the highest ranking probability for the occurrence of any TEAE, followed by fenfluramine and cannabidiol. The results of this pooled analysis suggest that stiripentol, fenfluramine, and cannabidiol are efficacious and safe add-on options for convulsive seizures in DS compared with placebo. In this indirect comparison, fenfluramine and stiripentol had comparable efficacy, while fenfluramine appeared to be safer. On the other hand, cannabidiol had a relatively lower efficacy and was associated with serious TEAEs.

- In 2021, Klein et al performed a meta-analysis of studies which compared the suicidality of newer antiseizure medications (ASMs) [i.e., eslicarbazepine, perampanel, brivaracetam, cannabidiol, and cenobamate] approved since 2008 with placebo. Suicidality was evaluated in 7 randomized clinical trials of these drugs, involving 5996 patients, of whom 4000 patients were treated with ASMs and 1996 with placebo. There was no evidence of increased risk of suicidal ideation (drugs vs placebo overall risk ratio, 0.75; 95% CI, 0.35-1.60) or attempt (risk ratio, 0.75; 95% CI, 0.30-1.87) overall or for any individual drug. Suicidal ideation occurred in 12 of 4000 patients treated with ASMs (0.30%) vs 7 of 1996 patients treated with placebo (0.35%) (p=0.74). Three patients treated with ASMs and no patients treated with placebo attempted suicide (p=0.22). Results of the meta-analysis indicate that overall there is no evidence of statistically significant increased risk of suicidal ideation (overall risk ratio, 0.75; 95% CI 0.35-1.60) or suicide attempt (risk ratio, 0.75; 95% CI, 0.30-1.87) in participants randomized to receive study ASM or placebo. This meta-analysis suggests that in patients with epilepsy without a history of suicidality, there is no

evidence that any of the 5 recently approved ASMs increase the risk of suicidality.

- In 2021, Zhang et al compared the efficacy and safety of antiseizure medications for Lennox–Gastaut syndrome (LGS) in a meta-analysis of randomized, controlled trials. A total of eight RCTs with 1171 patients were included in the network meta-analysis. There were 103 participants randomized to rufinamide in two RCTs, and 235 participants randomized to cannabidiol in two RCTs. In the remaining four RCTs, there were 48, 179, 79, and 37 participants assigned to topiramate, clobazam, lamotrigine, and felbamate, respectively. Even though all active ASMs were shown to be significantly superior to placebo with at least a 50% reduction in seizure frequency, surface under the cumulative ranking curve (SUCRA) suggested that rufinamide (83.8%), cannabidiol (68.5%), and topiramate (56.9%) were the three best ASMs in the ranking probability, followed by clobazam (47.3%) and lamotrigine (41.7%). The results demonstrated that except for topiramate, all other ASMs were markedly more effective than placebo; however, no significant difference was observed among the active treatments. The proportion of patients with at least a 75% reduction in drop seizures was reported in five RCTs. According to SUCRA, clobazam had the greatest likelihood, ranking first, and second was cannabidiol. Moreover, both were significantly superior to placebo in terms of this outcome (RR 3.74; 95% CI 1.14–12.24, p=0.029 and RR 3.46; 95% CI 1.18–10.19, p=0.024 respectively). According to SUCRA, lamotrigine (80.6%), cannabidiol (65.6%), and felbamate (59.4%) had the highest probabilities of being worse for serious adverse events. However, cannabidiol was the only treatment that had a significantly greater incidence of serious adverse events than placebo (RR 2.84; 95% CI 1.21–6.64, p=0.016). No substantial difference was observed between these active ASMs. Regarding dropouts, cannabidiol had the greatest possibility of ranking worst, with a SUCRA of 88.2%. The proportion of patients receiving cannabidiol were significantly greater than those receiving lamotrigine (RR 10.13; 95% CI 1.58–64.86, p=0.014), clobazam (RR 6.21; 95% CI 1.47–26.22, p=0.013), and placebo (RR 4.95; 95% CI 1.37–17.85, p=0.015). The results of this meta-analysis suggest that all ASMs demonstrated a significantly greater response rate than placebo. SUCRA ranking suggested that rufinamide and cannabidiol are more efficacious than other treatments in reducing seizures.
- In 2021, Jingxuan et al published a systematic literature review and meta-analysis of pharmacotherapy for the treatment of painful diabetic peripheral neuropathy (pDPN). Thirty-seven RCTs on pDPN published between January 1, 2008, and January 1, 2021, were included. Among them, 32.4% evaluated pregabalin, 10.8% evaluated duloxetine, 10.8% evaluated capsaicin, and 8.1% evaluated tapentadol, ABT-894, ABT-594 and clonidine. Compared with patients receiving placebo, those receiving

pregabalin [SMD −0.48, −0.11, p=0.002] and duloxetine [SMD −0.27 (95% CI −0.39, −0.15), p<0.00001], capsaicin [SMD −0.23 (95% CI −0.36), 0.09), p<0.0001], tapentadol [SMD −0.52 (95% CI −0.93, 0.11), p=0.01], mirogabalin [SMD −0.17 (95% CI −0.31, −0.04), p=0.01], and lacosamide [SMD −0.23 (95% CI −0.41, −0.04), p=0.02] had significantly lower pain scores. Patients receiving ABT - 894 [SMD 0.04 (95% CI 0.20, 0.27), p = 0.76] and gabapentin [SMD −0.25 (95% CI −0.54, 0.04), p=0.0)] had no significant difference in pain scores compared with those receiving placebo. Six medicines could also elicit a 50% pain reduction, among which pregabalin [RR 1.32 (95% CI 1.10, 1.58, p=0.003), duloxetine [RR 1.43 (95% CI 1.01, 2.02, p<0.04), and tapentadol [RR 1.38 (95% CI 1.12,1.71, p=0.003) had a significantly greater 50% pain reduction than placebo, while capsaicin [RR 0.99 (95% CI 0.73,1.36, p=0.97), mirogabalin [RR 1.02 (95% CI 0.69, 1.51, p=0.92), and gabapentin [RR 2.39 (95% CI 0.57, 10.00, p=0.23) showed no significant difference from placebo. The meta-analysis demonstrated that patients taking pregabalin [RR 1.29 (95% CI 1.07, 1.55), p=0.008], duloxetine [RR 1.16 (95% CI 1.08, 1.26), p=0.00002], capsaicin [RR 1.55 (95% CI 1.23, 1.97), p=0.0002], and tapentadol [RR 1.33 (95% CI 1.19, 1.48), p<0.00001] were more likely to report adverse events than the placebo group. In addition, ABT-894 [RR 0.94 (95% CI, 0.77, 1.16), p=0.56], gabapentin (RR 1.12 95% CI 0.97, 1.29, p=0.11), and lacosamide (RR 1.03, 95% CI 0.89, 1.19, p=0.69) demonstrated no statistically significant differences in terms of the risk of adverse events compared with placebo. These results suggest that pregabalin, duloxetine and tapentadol have good efficacy in the treatment of DPN pain. These three drugs are also the most common drugs for the clinical treatment of painful DPN at present.

- In 2021, Kishi et al published a massive meta-analysis of randomized, double-blind trials to compare the efficacy, acceptability, tolerability, and safety of pharmacological interventions for adults with acute bipolar mania. A total of 72 double-blinded RCTs (n = 16442, males = 50.93%, mean age = 39.55 years, mean study duration = 3.96 ± 2.39 weeks) were included with the following treatment arms (number of studies (N)/individuals (n)): aripiprazole (9/1205), asenapine (3/620), brexpiprazole (2/321), carbamazepine (6/305), cariprazine (3/612), chlorpromazine (1/10), endoxifen (2/55), eslicarbazepine (2/148), haloperidol (10/1023), lamotrigine (3/173), licarbazepine (1/324), lithium (20/965), olanzapine (14/1565), oxcarbazepine (1/30), paliperidone (2/542), quetiapine (5/630), risperidone (7/676), tamoxifen (2/43), topiramate (4/659), valnoctamide (1/71), valproate (14/981), verapamil (1/17), ziprasidone (3/458), and a placebo (48/5009). Aripiprazole, asenapine, carbamazepine, cariprazine, haloperidol, lithium, olanzapine, paliperidone, quetiapine, risperidone, tamoxifen, valproate, and ziprasidone showed a superior response to treatment than the placebo

(N = 56, n = 14503); the RR (95% CI) ranged from 7.461 (1.876, 29.678) for tamoxifen to 1.281 (1.049, 1.563) for asenapine. Compared with the placebo, aripiprazole, olanzapine, quetiapine, and risperidone had lower all-cause discontinuation (RR [95% CI] ranged from 0.647 [0.552–0.758] for olanzapine to 0.840 [0.719–0.980] for aripiprazole; N = 70, n = 16324), whereas topiramate had higher all-cause discontinuation (1.335 [1.032–1.728]). Compared with the placebo, aripiprazole, asenapine, carbamazepine, cariprazine, haloperidol, lithium, olanzapine, paliperidone, quetiapine, risperidone, valproate, and ziprasidone had lower discontinuation due to inefficacy, with the RR (95% CI) ranging from 0.349 (0.216 –0.564) for paliperidone to 0.716 (0.534 –0.961) for lithium (N = 50, n = 14284). Aripiprazole, asenapine, cariprazine, haloperidol, lithium, olanzapine, paliperidone, quetiapine, risperidone, and tamoxifen outperformed placebo for clinical remission (N=31, n=9320); the RR (95% CI) ranged from 8.441 (1.116, 63.841) for tamoxifen to 1.259 (1.007, 1.576) and for lithium. Compared with the placebo, asenapine (RR [95% CI] = 1.896 [1.117 –3.218]), haloperidol (1.867 [1.255 –2.776]), and lithium (1.791 [1.093 –2.936]) had higher discontinuation due to adverse events (N=52, n=14629), while olanzapine had lower discontinuation due to withdrawal consent (0.643 [0.466–0.889], N=42, n=11968). The results of this meta-analysis suggest that carbamazepine, lithium, tamoxifen, and valproate were effective for acute mania. However, only aripiprazole, olanzapine, quetiapine, and risperidone had better acceptability than the placebo.

- On June 15, 2022, and FDA notice was released indicating that diazepam rectal gel is currently on backorder and unavailable. This notice also indicated that there are no plans to manufacture Diastat® Rectal Gel or Diastat® Acudial. All volumes converted to the generic version.

Recommendation:

- Add Eprontia ™ (topiramate) oral solution to non-preferred.
- Remove Peganone® (ethotoin) tablets. They have been discontinued.
- Add Lacosamide (compare to Vimpat®) tablets and oral solution to preferred.
- Move Levetiracetam ER tablets to preferred.
- Move Topiramate ER sprinkle caps to non-preferred and grandfather existing users.
    - Clinical criteria:
        - Add Vimpat to the Carbatrol, Depakote, Depakote ER, Depakote Sprinkles, Dilantin, Keppra tablets or oral solution, Klonopin, Klonopin Wafers, Lamictal tablets or chew tablets, Lyrica, Mysoline, Neurontin capsules, tablets, solution, Onfi, Phenytek, Tegretol tablets, Tegretol XR (200 mg & 400 mg), Topamax tabs, Topamax sprinkles, Trileptal tablets, Trileptal oral suspension, Zarontin criteria.

- Add Eprontia: The patient has a medical necessity for a specialty dosage form.
- Add Qudexy XR, Topiramate ER, Trokendi XR to the Elepsia XR, Keppra XR, Lamictal XR, Lamotrigine ER, Levetiracetam ER, Oxtellar XR criteria with added note If topiramate ER is requested, the patient must have a documented intolerance to Qudexy.

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- **Ophthalmic Antibiotics**
  - No new drugs.
  - No other significant clinical changes.

Recommendation:

- Remove Moxeza® (moxifloxacin 0.5%) (preservative free) solution from the PDL. It has been discontinued.
- Add Moxifloxacin 0.5% (compare to Moxeza®) (preservative free) solution to non-preferred.

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- **Ophthalmic Allergic Conjunctivitis**
  - No new drugs.
  - No other significant clinical changes.

Recommendation:

- Add Bepotastine (compare to Bepreve®) to non-preferred.
  - Clinical Criteria:
    - Update Bepotastine, Bepreve, Epinastine: The patient has had a documented side effect, allergy, or treatment failure to a preferred ophthalmic antihistamine AND for approval of Bepotastine, the patient must have a documented intolerance to brand Bepreve.
    - Update Lastacaft: The patient is pregnant, and the diagnosis is allergic conjunctivitis OR The patient has had a documented side effect, allergy, or treatment failure to a preferred ophthalmic antihistamine.

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- **Ophthalmic Glaucoma Agents**
  - No new drugs.
  - No other significant clinical changes.

Recommendation:

- Add Brimonidine tartrate/timolol maleate (compare to Combigan®) and Travoprost BAK Free (compare to Travatan Z®) to non-preferred.
  - Clinical criteria:
    - Add Brimonidine/timolol: the patient must have a documented intolerance to brand Combigan.
    - Add Travoprost, to the Bimatoprost, Vyzulta, Xalatan, Xelpros, Zioptan criteria.

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- **Ophthalmic Dry Eye Agents**
  - No new drugs.
  - No other significant clinical changes.

Recommendation:

- No changes.

Public Comments: No public comment.

Board Decision: None needed.

- **Ophthalmic Anti-Inflammatory**
  - No new drugs.
  - No other significant clinical changes.

Recommendation:

- Add Difluprednate (compare to Durezol®) to non-preferred.

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- **Stimulants and Related Agents**
  - No new drugs.
  - The FDA labeling of Atomoxetine (Strattera®) was updated in 2022 to include warnings about the risk of new psychotic or manic symptoms

as well as aggressive behavior and hostility. Additional recent warnings recommend screening patients for bipolar disorder before initiating therapy with Atomoxetine (Strattera®).
    - The FDA labeling of lisdexamfetamine (Vyvanse®) was updated in 2021 to include a warning of growth suppression and a recommendation to monitor height and weight in pediatric patients during treatment.
    - Concerta® (methylphenidate SA OSM IR/ER, 22:78%) 36mg has been on product allocation since March 2022. Change Healthcare is routinely contacting the manufacturer for additional updates. There are no supply issues with other strengths.

Recommendation:

ADHD and Narcolepsy /Long-Acting Stimulants:

- Move FOCALIN® XR (dexmethylphenidate SR 24 HRIR/ER, 50:50%) to non-preferred.
- Add Methylphenidate DR 24HR IR/ER, 40:60% (compare to Aptensio®XR) to non-preferred.
- Add Relexxii® (methylphenidate ER OSM) IR/ER, 22:78% to non-preferred.
    - Clinical criteria:
        - Revise Aptensio XR, Methylphenidate DR 40:60: patient has had a documented side effect, allergy, or treatment failure on two preferred long-acting Methylphenidate products. For approval of Methylphenidate DR 40:60, the patient must also have a documented intolerance to brand Aptensio XR.
        - Add Focalin XR: the patient must have a documented intolerance to the generic equivalent.
        - Add Relexxi: Both Concerta and methylphenidate SA OSM must be on a long-term backorder and unavailable from the manufacturer.

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- **Sickle Cell Anemia**
    - No new drugs.
    - In December 2021, the FDA granted accelerated approval of a supplemental New Drug Application (sNDA) for Oxbryta® (voxelotor) tablets for the treatment of sickle cell disease (SCD) in children ages 4 to less than 12 years. This approval expands the previously approved use of Oxbryta to treat SCD in patients ages 12 years and older in the United States. The FDA also approved Global Blood Therapeutics' separate New Drug Application (NDA) for Oxbryta (voxelotor) tablets for oral suspension, a new dispersible, once-daily tablet dosage form

suitable for patients ages 4 to less than 12 years as well as for older patients who have difficulty swallowing whole tablets.
    - Howard et al 2021 Long-term analysis of HOPE, a randomized, double-blind, placebo-controlled, phase 3 multicenter study. The primary endpoint, the proportion who achieved a hemoglobin response at week 24, was already reported. At week 72, the adjusted mean change in hemoglobin from baseline was 1.0g/dL in the 1500mg group, 0.5g/dL in the 900mg group, and 0g/dL in the placebo group, with a significant difference observed between the 1500mg group and placebo($p<0.0001$) and between the 900mg group and placebo ($p=0.014$).

Recommendation:

- Add Oxbryta® 300mg tablets for oral suspension to non-preferred.
    - Clinical criteria:
        - Revise Oxbryta: Patient has a diagnosis of Sickle Cell Disease AND patient is at least 4 years of age or older AND patient has a baseline hemoglobin (Hb) ≤ 10.5 g/dL AND patient has had an inadequate response to a 6 month trial of hydroxyurea dosed at 15-35 mg/kg/day, unless contraindicated AND patient has experienced at least 2 vaso-occlusive crises in the previous 12 months despite compliance with hydroxyurea. Initial approval will be granted for 6 months. For re-approval, the patient must have a decrease in the frequency or severity of VOC compared to baseline.

Public Comments: Santreis Booze from Global Blood Therapeutics highlighted the attributes of Oxbryta®.

Board Decision: The Board unanimously approved the above recommendations.

12. Review of Newly-Developed/Revised Criteria:

- None at this time.

13. General Announcements:

- None at this time.

14. Adjourn: Meeting adjourned at 8:00 p.m.