Department of Vermont Health Access
Pharmacy Benefits Management Program
DUR Board Meeting
Draft Minutes

February 20, 2024: 6:00 – 8:30 p.m.

Board Members Present:

	Andy Miller, RPH		**Lucy Miller, MD**		**Douglas Franzoni, PharmD**
	Mark Pasanen, MD		**Anne Daly, PharmD**		**Louise Rosales, APRN**
	Rima Carlson, MD				

Board Members Absent:

	Bram Starr, MD		**Margot Kagan, Pharm D**		**Katharina Cahill, PharmD**

DVHA Staff Present:

	Stacey Baker		**Lisa Hurteau, PharmD**		**Ashley MacWalters**
	Taylor Robichaud, PharmD		**Michael Rapaport, MD**		

Change Healthcare Staff Present:

	Jacquelyn Hedlund, MD		**Laurie Brady, RPh**		

Guests/Members of the Public:

Alain Nguyen, Amy Atkins, Bill Eicholzer, Brian Denger, Brielle Dozier, Lauren Faricy, Frank Lanotte, I. Oko, Ingrid Ma, Kellyn Madden, Kim Witte, Kristen Chop, Laurie Ritchie, Laurie Webb, Marit Sivertson, Jim McCarthy, Nate Plasman, Nicole Pinkerton, Nikhil Kacker, Paul Isikwe, Nicholas Primpas, Collin Sinclair, Stephanie Kennedy, Annie Vong, Amy Cunningham, Ryan Miller, Chad Bohigian, Tim McSherry, Eric Sherr, Tina McCann, Jai Persico, Adam Denmon, Erin Booth, Mary Nadon Scott.

Executive Session

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

Introductions and Approval of DUR Board Minutes

- Attendance was called and introductions of DVHA and Change Healthcare Staff were made.
- The December 2023 meeting minutes were accepted as printed.
- Lisa Hurteau welcomed new board member, Rima Carlson, MD. She is a family medicine physician with Integrative Family Medicine in Montpelier.

DVHA Pharmacy Administration Updates: Lisa Hurteau, PharmD, DVHA

- Testimony was presented to the Senate Committee on Finance, January 24, 2024 for S.164: An act relating to health insurance coverage for obesity care.
- According to the Vermont Department of Health's Behavioral Risk Factor Surveillance System Report for 2022: Over one quarter (27%) of adult Vermonters live with obesity.
    - Over one third (35%) are overweight.
    - We anticipate a similar (or higher) percentage of Medicaid members being eligible for coverage.
- Bariatric Surgery is currently covered, but medications and comprehensive lifestyle intervention programs are not.
- Starting in 2023, DVHA's clinical and pharmacy teams, along with the Department's Chief Medical Officer, have convened a standing working group to examine the issue of Medicaid coverage for obesity medications. The goal of this group is to conduct cost-benefit analysis of weight loss treatment options for the Vermont Medicaid population, to pave the way for personalized and sustainable solutions in obesity management. DVHA is moving quickly to expedite the work of the obesity medication working group, using their review boards (CURB and DURB) to assist in forming recommendations.
- Preliminary cost data, using values reported as gross pharmaceutical costs based on Wholesale Acquisition Cost (WAC) price, are as follows. Net costs to DVHA may be lower based on federal and supplemental rebates.
    - 0.31% Patient Uptake (first year) would represent 156 members with a gross monthly cost of $200,000 and an annual cost of $2,400,000.
    - 0.87% Patient Uptake would represent 438 members with a gross monthly cost of $550,000 and an annual cost of $6,600,000.
    - 5% Patient Uptake (steady state volume) would represent 2,519 members with a gross monthly cost of $3,150,000 and an annual cost of $38,000,000.
    - 10% Patient Uptake (estimated future uptake) would represent 5,038 members with a gross monthly cost $6,300,000 and annual cost of $75,600,00.

Board Discussion:

- A board member asked if other states are covering anti-obesity medications. DVHA advised that Massachusetts began covering at the beginning of this year. North Carolina previously covered but recently stopped due to high costs, noting this was their state employee plan not their Medicaid plan. Change Healthcare states, Pennsylvania and Mississippi also recently began covering these agents.
- A board member advised that they have received many inquiries from patients regarding coverage of anti-obesity medications. Some patients have had amazing results, but they felt that DVHA should consider limiting coverage to the highest risk patients. Then noted that the most benefit is likely in patients with higher BMI's than the FDA indications.
- A board member noted that lifestyle modifications are difficult to support for most practices.

- A board member noted that this is uncharted territory and long-term outcomes data for these agents is lacking, and results can vary significantly between patients.

DVHA Chief Medical Officer Update

- None at this time

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

- Flovent HFA® (fluticasone propionate) Discontinuation
  - Inhaled Corticosteroids and Combinations
    Recommendation:
    - Add Asmanex® (mometasone furoate) HFA with QTY LIMIT: 3 inhalers (39 gm)/90 days to preferred for Age ≤ 11 years.
    - Add Fluticasone propionate HFA (compare to Flovent® HFA) with QTY LIMIT: 3 inhalers (36 gm)/90 days to preferred for Age ≤ 5 years.
    - Add Fluticasone propionate Diskus (compare to Flovent® Diskus) with QTY LIMIT: 180 blisters/90 days) and Breyna™ (budesonide/formoterol) with QTY LIMIT: 9 inhalers (92.7gm)/90 days to non-preferred.
      - Clinical criteria:
        - Add Armonair Digihaler, Alvesco, Fluticasone Diskus: The patient has had a documented side effect, allergy, or treatment failure to at least two preferred agents.
        - Add Asmanex HFA (Age ≥ 12 years): Medical necessity for the use of an HFA formulation has been provided.
        - Add Fluticasone HFA (Age ≥ 6 years): The patient has had a documented side effect, allergy, or treatment failure to at least two preferred agents, one of which must be Asmanex HFA OR Medical necessity for the use of an HFA formulation has been provided and the patient has a documented side effect, allergy, or treatment failure to Asmanex HFA.
        - Add Breyna, Budesonide/formoterol: the patient has a documented intolerance to brand Symbicort.

Public Comment: Lauren Faricy, MD, Pediatric Pulmonologist from University of Vermont Medical Center thanked the board for their consideration of expanding the age for preferred status of Asmanex® HFA (mometasone furoate). She advised this will help improve some of the difficulties they have encountered managing younger patients. She also noted that although she has heard about issues with backorders of Asmanex® HFA nationwide, they have not experienced any issues with their New York and Vermont patients.

Board Decision: The Board unanimously approved the above recommendations.

RetroDUR/Pro DUR: **Jacqueline Hedlund, MD Change Healthcare and Laurie Brady, RPh Change Healthcare**

- Follow-Up: Co-prescribing of Opioids, Benzodiazepines, and Skeletal Muscle Relaxants

The co-prescribing of opioids, benzodiazepines, and muscle relaxants is known to cause significant morbidity and has been shown to increase the likelihood of hospital admissions. A retrospective cohort study was published in 2019, examining data from the Medical Expenditure Panel Survey longitudinal dataset and the affiliated Prescribed Medicines Files from 2013-2014, weighted to reflect the actual US population. The results showed that 0.53% of the population used all three classes of medications simultaneously and compared with non-users, the odds ratio of hospitalization was 8.52 in 2013. Respiratory and CNS depression are the primary reasons for hospitalizations and deaths associated with concurrent use. A study completed in Washington State found that opioid users had a 12-fold increased rate of death when also taking a benzodiazepine and muscle relaxant. While the FDA has issued warnings about the combined use of benzodiazepines and opioids, adding a muscle relaxant contributes to the risk of hospitalization and poor outcomes. Short-term use of opioid and benzodiazepine drugs has been deemed reasonable in specific situations, although the use of triple drug therapy with opioids, benzodiazepines, and muscle relaxants, even in the short-term, is not considered appropriate patient care. FDA Warnings about the co- prescribing of benzodiazepines and opioids has brought attention to the risks; however, short-term overlapping prescriptions are sometimes seen, although less frequently over the last few years.

Change Healthcare used paid, non-reversed Medicaid pharmacy claims from Calendar Year 2022, excluding members with Part D, VMAP and Healthy Vermonters coverage. They identified members who were prescribed an opioid, benzodiazepine, and muscle relaxant with overlapping dates of service and determined if the members had the same or different prescribers. Of note, substance use disorder treatments (e.g. buprenorphine) and methadone obtained from an Opioid Treatment Program (OTP) were not included.

There were 17,095 members on any 3 of the drug classes of which 195 members had overlapping claims for opioids, benzodiazepines, and muscle relaxants (1.14%). When analyzing all members in the studied population, the average number of overlapping days was 62 for calendar year 2022. Of the 195 members prescribed triple drug overlap, 10 (5.1%) were on 3 overlapping drugs for 280 days or more, and 23 (11.8%) were on 180 days or more. When analyzing all members in the studied population, the average number of overlapping days was 62 for calendar year 2022. Of the 195 members prescribed triple drug overlap, 10 (5.1%) were on 3 overlapping drugs for 280 days or more, 23 (11.8%) were on 180 days or more of the three studied overlapping drug classes.

Recommendation:
There is a concern that over 44% (86 unique members) of those prescribed drugs from all three studied classes were seen by different prescribers for their prescriptions. This suggests that either incomplete history and medication reconciliations were completed or that there is an unawareness of the risks of taking a drug from all three classes concurrently. A sample chart review by DHVA may be helpful to determine member diagnoses and to evaluate prescriber

documentation that would clinically support the necessity of triple therapy in these members. Additionally, a targeted provider outreach, with the greatest priority given to prescribers in the "Different" studied population, may assist with provider notification and awareness among their patient population. Most of the members were getting all three prescriptions filled at the same pharmacy. Notifications to pharmacies who are filling these prescriptions may be in order to remind them of the inherent danger of taking medications from the 3 drug classes simultaneously.

Board Discussion: A board member explained that their practice may have a few patients on two or three of these medications. However, they are prescribed by different specialties, and necessary for the specified diagnosis.

- Data presentation: GLP-1 Receptor Agonist Adherence

The medications in the GLP-1 receptor agonist drug class are an important addition to the available treatments for type 2 diabetes. Their mechanisms of action include augmentation of insulin secretion, suppression of glucagon secretion, deceleration of gastric emptying, and reduction of calorie intake and body weight. In addition to controlling glucose levels and reducing hemoglobin A1c levels, the drugs have been shown to have a significant reduction in major adverse cardiovascular events (MACE) in those with cardiovascular disease and induce significant weight loss. The American Diabetes Association (ADA) guidelines now suggest using GLP-1 agonists preferentially over insulin in those who do not reach goal A1c targets with oral therapy. The GLP-1 receptor agonists are given subcutaneously, either twice a day, once a day, or once weekly. However, compliance with the medications has presented as a possible concern. The available data in the Medicaid population is limited, but an analysis of adults in the U.S. showed overall 50.9% and 47.4% of patients were adherent to GLP-1 therapy at 12 months and 24 months, respectively. The common side effects of these medications includes: nausea, vomiting, and diarrhea, and serious side effects include bowel obstructions. In addition, some people with type 2 diabetes do not respond to the drugs. In commercially insured patients, costs have been shown to be a factor in discontinuation rates due to high out of pocket costs.

Change Healthcare used paid, non-reversed Medicaid pharmacy claims from calendar year 2022 to evaluate the number of members initiating GLP-1 medications, excluding members with Part D, VMAP and Healthy Vermonters coverage. The same claims analysis was completed for 2023 to evaluate medication adherence and discontinuation rates. Members were screened for continuous eligibility, those that remained covered by Vermont Medicaid for the entirety of calendar year 2023 were included in the review.

Change Healthcare reviewed Vermont paid, non-reversed pharmacy claims in members on GLP-1 receptor agonists. For the members included in the analysis; the reviewers looked at the numbers of members that remained on a GLP-1 medication at months 3, 6, 9 and 12, from the time of the first claim. Additionally, the reviewers examined the medication possession ratio (MPR) to see how many members where adherent to the medications, as prescribed. An

acceptable value of 80% or greater was used as an MPR to be considered adherent with the prescribed regimen. The results of this analysis show that at 1 year from therapy initiation, starting in CY2022, only 59% of Vermont Medicaid members continued utilizing GLP-1 drugs. After a subgroup review of the 435 members that remained on GLP-1 drugs after 1 year, it was determined that 77% where within acceptable ranges for adherence, described by MPR values.

Recommendation: Adherence is an important consideration when reviewing health outcomes related to a drug class. Due to the variable side effects of these medications, patients should be educated appropriately and titrated slowly to therapeutic response. The recommendation, as a result of this analysis, is to consider the discontinuation rates for GLP-1 drugs when evaluating the use of these products for all indications (e.g. type 2 diabetes, weight loss). When used for weight loss, clinical trials have shown that long-term use will be needed to prevent treatment failure and weight regain. The discontinuation rates commonly seen within this class may have a significant relationship with the expected health outcomes and benefits. Further research is warranted to detail the long-term health outcomes, when weighed against the discontinuation rates, for GLP-1 drugs as a class.

Board Discussion: A board member felt that the adherence data presented may have been influenced by difficulties with product availability. They have experienced many supply issues over the past few years which have required patients to change products or doses frequently. The board asked if DVHA could look at one of the first GLP-1 drugs and cross reference its usage to current time or repeat this analysis after supply issues are resolved.

- Introduce: The Effect of Hemlibra® (emicizumab-kxwh) on the Cost of Care in Hemophilia A Patients

Hemlibra® (emicizumab-kxwh), a bispecific - and factor X -directed antibody is used to treat factor VIII deficient patients (hemophilia A), with or without inhibitors. It activates the coagulation cascade downstream of the factor VIII activating pathway, thereby negating the need for factor VIII for normal coagulation. It was initially developed for patients with inhibitors to factor VIII, which usually develop after only a few exposures to factor products, to reduce the need for immune tolerance with very high doses of factor and to avoid the use of bypassing agents, such as NovoSeven® (coagulation Factor VIIa, recombinant). However, it is now routinely used as the initial prophylactic treatment in children born with hemophilia, due to the ease of subcutaneous administration and only rare incidences of inhibitor development. If bleeding occurs, traditional factor replacement is used. Hemlibra® may be given weekly, every other week, or monthly. In children, it prevents the need for central line placement, which poses risks of infection. Additionally, there is no longer a need for IV prophylaxis several times a week. The medical and scientific advisory council (MASAC) of the National Bleeding Disorders Foundation recommends Hemlibra® as one possible prophylactic agent for the treatment of patients with factor VIII deficiency. While Hemlibra® is more costly per month than traditional factor infusions, it is possible that the overall cost of care for patients is decreased, due to better compliance with prophylaxis (no IV required), less development of inhibitors, which are more costly to treat, and less use of medical care, including: hospitalizations for infections from

central lines, bleeds, and trauma-related care. Note: Hemlibra® was FDA approved in November 2017 for adults and children with hemophilia A with factor VIII inhibitors. Its approval was extended in October 2018 to hemophilia A patients without FVIII inhibitors.

We will use paid, non-reversed Vermont Medicaid pharmacy and medical claims, excluding members with Part D, VMAP and Healthy Vermonters coverage. The dates analyzed will be specific to each patient and determined from the treatment initiation period.

For members taking Hemlibra®, we will analyze medical and pharmacy claims. The analysis will look at the number and cost of hospitalizations, ER visits, factor use/prescription drug use (pharmacy claims and medical benefit claims), and provider visits for the year prior to starting Hemlibra® and 1-2 years after starting the medication. In those who have been on traditional factor VIII prophylaxis prior to starting Hemlibra®, we will calculate to see if the increased cost of Hemlibra® is offset by decreased utilization of medical care, including factor use. The following Factor VIII Therapies will be included in the analysis: Advate®, Adynovate®, Afstyla®, Alphanate®, Eloctate®, Esperoct®, Helixate® FS, Hemofil®-M, Humate-P®, Jivi®, Koate®-DVI, Kogenate®, Kovaltry®, Monoclate®-P, NovoEight®, Nuwiq®, Recombinate®, Wilate®, Xyntha®

Clinical Update: Drug Reviews: Jacqueline Hedlund, MD, and Laurie Brady, RPh, Change Healthcare

Biosimilar Drug Reviews

- None at this time

Full New Drug Reviews

- Elevidys® (delandistrogene moxeparvovec-rokl)

Delandistrogene moxeparvovec-rokl, the active ingredient of Elevidys®, is a recombinant gene therapy designed to deliver the gene encoding the Elevidys® micro-dystrophin protein. Elevidys® is the recombinant gene therapy product that is comprised of a non-replicating, recombinant, adeno-associated virus (AAV) serotype rh74 (AAVrh74) capsid and a ssDNA expression cassette flanked by inverted terminal repeats (ITRs) derived from AAV2. The cassette contains: 1.) an MHCK7 gene regulatory component comprising a creatine kinase 7 promoter and an α-myosin heavy chain enhancer, and 2.) the DNA transgene encoding the engineered Elevidys® micro-dystrophin protein. It is indicated for the treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene. This indication is approved under accelerated approval based on expression of Elevidys® micro-dystrophin observed in patients treated with Elevidys®. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). This indication is approved under accelerated approval based on expression of Elevidys® micro-dystrophin in skeletal muscle observed in patients treated with Elevidys®. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). Use is contraindicated in patients with any deletion in exon 8 and/or exon 9 in the DMD gene. Prior to use, assess liver function, obtain platelet counts and troponin-I levels, and postpone infusion in patients with

infections until the infection has resolved. In addition, measure baseline anti-AAVrh74 antibody titers. Accelerated approval was based on data from Study 1 and Study 2, both of which are ongoing studies. The primary objectives of Study 1 were to evaluate expression of Elevidys® micro-dystrophin in skeletal muscle, as well as to evaluate the effect of Elevidys® on the NSAA total score. Changes from baseline in Elevidys® micro-dystrophin expression per Western blot were statistically significant, which was also noted in Study 2. The change in NSAA total score was not statistically significant between Elevidys® and placebo at week 48 in Study 1. It is recommended that Elevidys® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

Recommendation:

- Add Elevidys® (delandistrogene moxeparvovec-rokl) to non-preferred.
    - Clinical Criteria:
        - Add Elevidys: The patient is 4 to 5 years of age AND
        - The patient is ambulatory, and results of the North Star Ambulatory Assessment (NSAA) have been provided AND
        - The patient must have a diagnosis of Duchenne Muscular Dystrophy with either a confirmed frameshift mutation, or a premature stop codon mutation between exons 18 to 58 in the DMD gene AND
        - The patient does not have a deletion in exon 8 or 9 of the DMD gene. AND
        - The baseline anti-AAVrh74 antibody titer results are <1:400, using a Total Binding Antibody enzyme-linked immunosorbent assay (ELISA). AND
        - The patient is not on concomitant DMD antisense oligonucleotide therapy (e.g. golodirsen, casimersen, viltolarsen, eteplirsen) AND
        - The patient is on a stable dose of corticosteroids for at least 12 weeks prior to Elevidys infusion AND
        - Prescriber attests to complete the following:
            - Assess liver function (clinical exam, GGT, and total bilirubin) at baseline and weekly for the first 3 months. Continue monitoring if clinically indicated, until results are unremarkable normal clinical exam, GGT, and total bilirubin levels return to near baseline levels).
            - Obtain platelet counts at baseline and weekly for the first two weeks.
            - Obtain troponin-I at baseline and weekly for the first month.
        - Approval will be granted for a maximum of one dose per lifetime and may not be renewed.

Public Speaker:

- Stephanie Kennedy, PharmD, MBA, Sarepta Therapeutics, highlighted the attributes of Elevidys. Stephanie Requested that the board consider removing the requirement that the patient must be on a stable corticosteroid dose for at least 12 weeks. She also

requested that the board consider coverage in patients with a mutation in exons 1-17 and 59-71 of the DMD gene.
- Laurie Webb, Member of Public, spoke on her thoughts about Elevidys and advocated for coverage.
- Brian Denger, Parent Project Muscular Dystrophy, spoke on his thoughts about Elevidys and advocated for coverage.
- Nate Plasman, Member of Public, spoke on his thoughts about Elevidys and advocated for coverage.
- Marit Sivertson, Member of Public, spoke on her thoughts about Elevidys and advocated for coverage.

Board Decision: A representative from Change Healthcare questioned how the FDA approved the treatment, without requiring patients to have 12 weeks of steroids, when every patient in clinical trials was on 12 weeks of steroids prior to administration. It was discussed that an expert panel of genetic specialist made this recommendation. The Board elected to remove the 12-week corticosteroid requirement from the criteria, leaving all other criteria as written and unanimously approved the modified recommendations. The board requested follow up discussion, after meeting with local specialists, to discuss the additions of broader coverage for exon mutations.

- Ngenla™ (somatrogon-ghla)

Somatrogon-ghla, the active ingredient of Ngenla®, is a human growth hormone analog. It is a fusion protein produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology. It is comprised of the amino acid sequence of human growth hormone (hGH) with one copy of the C-terminal peptide (CTP) from the beta chain of human chorionic gonadotropin at the N-terminus and 2 copies of CTP (in tandem) at the C-terminus. It is indicated for the treatment of pediatric patients aged 3 years and older who have growth failure due to an inadequate secretion of endogenous growth hormone. A multicenter, randomized, open-label, active-controlled, parallel-group, phase 3 study was conducted in treatment-naïve, prepubertal pediatric subjects with growth hormone deficiency. The primary efficacy endpoint was annualized height velocity at week 52, and results suggested that treatment with once-weekly Ngenla® for 52 weeks resulted in an annualized height velocity of 10.1 cm/year while treatment with daily somatropin achieved an annualized height velocity of 9.8 cm/year after 52 weeks of treatment. Per the full-text study by Deal et al, the authors concluded that the efficacy of once-weekly somatrogon was noninferior to once-daily somatropin, with similar safety and tolerability profiles.

Recommendation:
- Add Humatrope® and Ngenla™ (somatrogon-ghla) to non-preferred.
    - Clinical Criteria:
        - Update Humatrope, Nutropin AQ, Omnitrope, Saizen, Skytrofa, Zomacton: The patient has a documented side effect, allergy, or treatment failure to both preferred agents.
        - Update Ngenla, Sogroya: The patient has a documented side effect,

allergy, or treatment failure to both preferred agents AND the patient has a documented side effect, allergy, or treatment failure to Skytrofa.

Public Speaker: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- Opvee® (nalmefene)

Nalmefene, the active ingredient of Opvee®, is an opioid antagonist, a 6-methylene analogue of naltrexone. It is an antagonist at opioid receptors and it reverses the effects of natural and synthetic opioids, including respiratory depression, sedation, and hypotension. Pharmacodynamic studies have shown that nalmefene injection has a longer duration of action than naloxone injection at fully reversing doses. Nalmefene has no opioid agonist activity. It is indicated for the emergency treatment of known or suspected overdose induced by natural or synthetic opioids in adults and pediatric patients aged 12 years and older, as manifested by respiratory and/or central nervous system depression. Opvee® is intended for immediate administration as emergency therapy in settings where opioids may be present. It is not a substitute for emergency medical care. There were no clinical efficacy trials identified in the prescribing information for Opvee®. In a pharmacokinetic study that included healthy adults, the relative bioavailability of one 2.7mg Opvee® nasal spray in one nostril was compared to a single dose of nalmefene 1.0mg administered as an IM injection. The Tmax for Opvee® vs nalmefene IM was 0.250 hr vs 0.33 hr, while the half-life was 11.4 hrs vs 10.6 hrs, respectively. The AUC 0-10min was 0.523 vs 0.0639 ng-hr/ml, and the AUC 0-15min was 1.20 vs 0.142 ng-hr/ml. The nasal device does not need to be primed or assembled, as it is ready for use. Deliver one spray by intranasal administration and seek emergency medical assistance as soon as possible after administration of the first dose. Additional doses may be required. Head-to-head comparator efficacy trials with other agents were not identified.

Recommendation:

- Add Opvee® (nalmefene) nasal spray to non-preferred.
  - Clinical criteria:
    - Update Opvee, Zimhi: The prescriber must provide a clinically compelling reason why the preferred agents would not be suitable alternatives.

Public Speaker: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- Roctavian™ (valoctocogene roxaparvovec-rvox)

Valoctocogene roxaparvovec-rvox, the active ingredient of Roctavian™, is an adeno-associated virus (AAV) vector-based gene therapy product. Roctavian™ is an adeno-associated virus serotype 5 (AAV5) based gene therapy vector, designed to introduce a functional copy of a transgene encoding the B-domain deleted SQ form of human coagulation factor VIII (hFVIII-SQ). Transcription of this transgene occurs within the liver, using a liver-specific promoter, which

results in the expression of hFVIII-SQ. The expressed hFVIII-SQ replaces the missing coagulation factor VIII needed for effective hemostasis. It is indicated for an adeno-associated virus vector-based gene therapy for the treatment of adults with severe hemophilia A (congenital factor VIII deficiency with factor VIII activity <1 IU/dL) without antibodies to adeno- associated virus serotype 5 (AAV5) detected by an FDA-approved test. The efficacy of Roctavian™ was assessed in an open-label, single-dose, single-arm study that included adult males with severe hemophilia A. The primary efficacy outcome was a non-inferiority (NI) test of the difference in annualized bleeding rate (ABR) in the efficacy evaluation period following Roctavian™ administration compared with ABR during the baseline period in the rollover population. The non-inferiority (NI) margin was 3.5 bleeds per year. The mean efficacy evaluation period ABR was 2.6 bleeds per year after Roctavian™ treatment compared to a mean baseline ABR of 5.4 bleeds per year. The NI met the pre-specified NI margin, indicating the efficacy of Roctavian™.

Recommendation:

- Add Roctavian™ (valoctocogene roxaparvovec-rvox) to non-preferred.
    - Clinical criteria:
        - Add Criteria for all gene therapy products: The provider, healthcare facility, and patient will attest to continued clinical information exchange with The Department of Vermont Health Access, as is necessary to meet the terms of any value-based rebate agreements that have been entered into by The Department of Vermont Health Access. (e.g. patient response to therapy, clinical lab values to support treatment success/failure, annual follow up documentation)
        - Add Roctavian: Patient is ≥ 18 years of age AND Patient has a diagnosis of severe congenital Factor VIII deficiency, as evidenced by < 1% of normal circulating factor VIII AND Patient has the following:
            - Current and continuous use of Factor VIII prophylaxis therapy for the previous 12 months as evidenced by claims history or clinical documentation, without breaks in adherence. (Continuous use is defined as routine prophylaxis with defined frequency, e.g. twice weekly, once every two weeks) AND
            - Current or historical life-threatening hemorrhage despite use of preferred prophylaxis therapy OR Repeated, serious spontaneous bleeding episodes requiring hospitalization AND
        - Patient must be anti-AAV5 antibody negative.
        - Patient has been tested and found negative for Factor VIII inhibitor titers AND
        - The patient meets one of the following:
            - Patient is not HIV positive; or
            - Patient is HIV positive and is virally suppressed with anti-viral therapy (i.e., < 200 copies of HIV per mL) AND
        - The patient's hepatitis B surface antigen is negative AND
        - The patient meets one of the following:

        - Patient's hepatitis C virus (HCV) antibody is negative; or
        - Patient's HCV antibody is positive, and the patient's HCV RNA is negative AND
    - The patient is not currently using antiviral therapy for hepatitis B or C AND does not have significant liver dysfunction/significant fibrosis.
    - The patient does not have significant renal impairment (Creatinine ≥ 1.5 mg/dL)
    - Prescriber attests that the patient's ALT and factor VIII activity will be monitored weekly for at least 26 weeks following administration of Roctavian and regularly thereafter per the monitoring schedule recommended in the prescribing information.
    - Approval will be granted for a maximum of one dose per lifetime and may not be renewed.

Public Comment: Ingrid Ma, RPh, Pharm. D, from BioMarin Pharmaceuticals highlighted the attributes of Roctavian.

Board Decision: The Board unanimously approved the above recommendations.

- Skyclarys® (omaveloxolone)

Skyclarys® contains omaveloxolone; the precise mechanism by which it exerts its therapeutic effect in patients with Friedreich's ataxia is not known. Omaveloxolone have been shown to activate the Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway in vitro and in vivo in animals and humans. The Nrf2 pathway is involved in the cellular response to oxidative stress. It is indicated for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older. The safety and efficacy of Skyclarys® were assessed in a 48 week, randomized, double-blind, placebo-controlled study that included patients 16 to 40 years of age with Friedreich's ataxia. Treatment with Skyclarys® resulted in statistically significant lower mFARS scores (less impairment) as compared to placebo at week 48 in the population of patients without pes cavus (N=82). Similar results were obtained in the all randomized population, which included all patients regardless of pes cavus status, with a nominally significant least squares mean difference between treatment groups. The clinical significance of a 2.41 points difference on a 99-point rating scale, despite being statistically significant, is unclear. It is the first and only FDA-approved prescription medicine for this indication.

Recommendation:

- Add Skyclarys® (omaveloxolone) with QTY LIMIT: 3 capsules/day to non-preferred.
    - Clinical criteria:
        - Add Skyclarys:
            - The patient is ≥16 years of age
            - The patient has a diagnosis of Friedreich's Ataxia with a confirmed mutation in the frataxin (FXN) gene AND

- The patient must have a stable modified Friedreich's Ataxia Rating Scale (mFARS) score between 20 and 80, be able to complete maximal exercise testing, and have a left ventricular ejection fraction of at least 40%.
- Baseline liver function tests will be completed prior to start of therapy and continued monthly for 3 months following Skyclaris administration AND
- Baseline B-type natriuretic peptide (BNP) will be obtained, and level does not exceed 200pg/mL AND the patient has no history of clinically significant cardiac disease AND

- Reauthorization Criteria: For continuation, the patient must have a decrease in mFARS score compared to baseline.

Public Comment:

- Paul Isikwe, Pharm.D, MS, Biogen highlighted the attributes of Skyclarys and requested that mFARS score be removed from the criteria since this is not commonly done in clinical practice.
- Mary Nadon Scott, Member of Public, Friedreich's Ataxia Community, spoke on her thoughts about Skyclarys and advocated for coverage.

Board Discussion: A board member asked how long the initial approval would be for and Change Healthcare advised that all approvals are for 1 year, unless otherwise noted on the PDL. A board member requested that re-authorization approval be changed to state that there is slower or stable progression of the disease than would otherwise be expected. A representative from DVHA shared a link to the modified Friedreich's Ataxia Rating Scale.

Board Decision: A board member requested that re-authorization approval be changed to state that there is slower or stable progression of the disease than would otherwise be expected. The Board elected to change the criteria used for reauthorization, leaving all other criteria as written and unanimously approved the modified recommendations.

- Suflave™ (polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution)

Suflave® (polyethylene glycol [PEG] 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution) is an osmotic laxative. The primary mode of action is the osmotic effects of PEG 3350, sodium sulfate, and magnesium sulfate, which induce a laxative effect. The physiological consequence is increased water retention in the lumen of the colon, resulting in loose stools. It is indicated for the cleansing of the colon as a preparation for colonoscopy in adults. The colon cleansing efficacy of Suflave® was assessed in two randomized, single-blind, active-controlled, multicenter, studies (Study 1 and Study 2), that included adult patients undergoing colonoscopy for colorectal cancer screening and surveillance, or diagnostic colonoscopy, including patients with abdominal pain, diarrhea, constipation, and non-severe inflammatory bowel disease. Its efficacy was assessed in two randomized, single-blind, active-controlled, multicenter studies that included adult patients

undergoing colonoscopy for colorectal cancer screening and surveillance, or diagnostic colonoscopy. In both trials, the primary efficacy endpoint was the proportion with successful colon cleansing, and Suflave® was non-inferior to the active comparator in both studies.

Recommendation: Add Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate (compare to Suprep®) and Suflave™ to non-preferred.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Vyjuvek® (beremagene geperpavec-svdt)

Vyjuvek® (beremagene geperpavec-svdt) is a suspension of a herpes-simplex virus type 1 (HSV-1) vector-based gene therapy, mixed with the supplied sterile excipient gel for topical application on wounds. It is a live, replication defective HSV-1 based vector that has been genetically modified to express the human type VII collagen (COL7) protein. It is indicated for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene. The efficacy of Vyjuvek® gel was assessed in 31 subjects with DEB with mutation(s) in the COL7A1 gene in a randomized, double-blind, intra-subject placebo-controlled study. Efficacy was established on the basis of improved wound healing, defined as the difference in the proportion of complete (100%) wound closure at 24 weeks confirmed at two consecutive study visits two weeks apart (assessed at weeks 22 and 24 or at weeks 24 and 26). Significantly more complete wound closure occurred in the Vyjuvek® gel group as compared with the placebo gel group. Vyjuvek® is the first and only treatment that focuses on the genetic cause of DEB as a gel formulation for wound healing.

Recommendation:

- Add Vyjuvek® (beremagene geperpavec-svdt) to non-preferred.
    - Clinical criteria:
    - Add Vyjuvek:
        - The patient has a diagnosis of dystrophic epidermolysis bullosa (DEB) with confirmed mutation(s) in the collagen type VII alpha 1 chain COL7A1) gene AND
        - The patient does not have current evidence or history of squamous cell carcinoma or active infection in the area requiring Vyjuvek application. AND
        - The patient has used standard wound care treatments, including silicone or foam dressings without wound resolution AND
        - The intended wounds cover a large area of the patient's body OR are likely to present for an extended duration (e.g. months of healing) AND
        - The intended wounds have presented significant detrimental health consequences to the patient and are unlikely to be resolved with standard wound care management (e.g. hospitalizations, frequent

professional wound care management, significant quality of life disruptions) AND
- Approval will be limited to a maximum of 10 mL per 28 days
- Initial approval will be granted for 6 months. For reapproval, the patient must have a documented reduction in the number of wounds, decrease in wound size, increase in granulation tissue, or complete wound closure.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Vyvgart® Hytrulo (efgartigimod alfa and hyaluronidase-qvfc human recombinant injection)

Vyvgart® Hytrulo is a co-formulation of efgartigimod alfa and hyaluronidase (human recombinant). Efgartigimod alfa, a neonatal Fc receptor blocker, is a human immunoglobulin G1 (IgG1)-derived Fc fragment of the za allotype, produced in Chinese hamster ovary (CHO) cells. Hyaluronidase is an endoglycosidase used to increase the dispersion and absorption of co administered drugs when administered subcutaneously. Hyaluronidase (human recombinant) is a glycosylated single-chain protein produced by CHO cells containing a DNA plasmid encoding for a soluble fragment of human hyaluronidase (PH20). It is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. Study 1 (included in the prescribing information for Vyvgart® Hytrulo), which established the effectiveness of efgartigimod alfa-fcab for the treatment of gMG in adults who are AChR antibody positive, was conducted with efgartigimod alfa-fcab intravenous formulation (Vyvgart®). In study 2, Vyvgart® Hytrulo demonstrated a comparable pharmacodynamic effect on AChR antibody reaction as compared to the efgartigimod alfa-fcab IV formation, which established the efficacy of Vyvgart® Hytrulo. It is to be administered by a healthcare professional only and is for subcutaneous use only and administered with a winged infusion set. Vyvgart® Hytrulo demonstrated a comparable pharmacodynamic effect on AChR antibody reduction as compared to the efgartigimod alfa-fcab intravenous formulation (Vyvgart®), which established the efficacy of Vyvgart® Hytrulo.

Recommendation:
- Add Vyvgart® Hytrulo (efgartigimod alfa and hyaluronidase-qvfc human recombinant injection) SC solution to non-preferred.
  - Clinical criteria:
    - Update Vyvgart, Vyvgart Hytrulo:
    - Patient is ≥ 18 years of age AND
    - Patient has a diagnosis of generalized Myasthenia Gravis with Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV AND
    - Patient is anti-acetylcholine receptor (AChR) positive AND
    - MG-Activities of Daily Living (MG-ADL) total score of ≥5 at baseline AND

- Patient has IgG levels of at least 6g/L AND
- Patient has had an inadequate response with at least 2 immunosuppressive therapies (e.g. corticosteroids, azathioprine, cyclosporine, mycophenolate) over the course of at least 12 months AND
- Maximum of four doses per 50 days AND
- For approval of Vyvgart Hytrulo, the prescriber must provide a clinically compelling reason for the use of the requested medication including reasons why Vyvgart IV would not be a suitable alternative.
- For re-approval, the patient must have had a positive response to therapy as evidenced by a 2-point reduction in the MG-ADL score.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

New Managed Therapeutic Drug Classes

- None at this time

Therapeutic Drug Classes – Periodic Review

- Antibiotics/GI and Related

  Recommendation:

  - Clinical criteria:
    - Update Inflammatory Bowel Disease: Crohn's Disease (Xifaxan 550 mg or 200 mg Tablets): patient has a diagnosis of Crohn's Disease. AND Patient has had a documented side effect, allergy, treatment failure or contraindication to one of the following: 6- mercaptopurine, azathioprine, corticosteroids, or methotrexate. AND Quantity limit is 600 mg to 1,600 mg/day.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Antibiotics/Aminoglycosides

  Recommendation: No changes

- Antibiotics/Cephalosporins 1st Gen

  Recommendation: No changes

- Antibiotics/Cephalosporins 2nd Gen

Recommendation: Remove Cefaclor suspension. It is no longer available.

- Antibiotics/Cephalosporins 3rd Gen

  Recommendation:
  - Remove Suprax® (cefixime) chewable tablets and Suprax® (cefixime) suspension. They are no longer available.
  - Add Cefixime capsules to non-preferred.
    - Clinical criteria:
      - Patient is completing a course of therapy which was initiated in the hospital. OR patient has had a documented side effect or treatment failure to cefdinir or cefpodoxime.

- Antibiotics/Clindamycin

  Recommendation: No changes

- Antibiotics/Macrolides

  Recommendation: Remove quantity limits on Azithromycin

- Antibiotics/Nitrofurantoin Derivatives

  Recommendation: No changes

- Antibiotics/Oxazolidinones

  Recommendation:
  - Move Linezolid (compare to Zyvox®) tablets with QTY LIMIT:56 tablets per 28 days to preferred.
    - Clinical criteria:
      - Add Linezolid suspension, Zyvox suspension: The patient must have medical necessity for a liquid formulation (i.e. swallowing disorder). AND If the request is for generic linezolid suspension, the patient has a documented intolerance to brand Zyvox suspension.
      - Add Sivextro: patient has been started on Sivextro in the hospital and will be finishing the course of therapy in an outpatient setting OR patient has a documented blood, tissue, sputum, or urine culture that is positive for Vancomycin-Resistant Enterococcus (VRE) species. OR patient has a documented blood, sputum, tissue, or urine culture that is positive for Methicillin-Resistant Staphylococcus species AND patient has had a documented treatment failure with linezolid, trimethoprim/sulfamethoxazole, clindamycin, doxycycline, or

minocycline OR there is a clinically valid reason that the patient cannot be treated with one of those agents.
    - Add Zyvox tablets: the patient has a documented intolerance to generic linezolid tablets.

- Antibiotics/Penicillins

  Recommendation: No changes

- Antibiotics/Quinolones

  Recommendation: No changes

- Antibiotics/Tetracyclines

  Recommendation:
    - Remove Vibramycin® (doxycycline calcium) syrup. It is no longer available.
    - Remove Vibramycin® (doxycycline hyclate) suspension, Ximino® (minocycline) caps ER, and Oracea® (Doxycycline (Rosacea) Cap Delayed Release 40 MG) from the PDL. They are no longer rebateable.
    - Add minocycline ER tablets (compare to Solodyn®) to non-preferred.
        - Clinical criteria:
            - Patient has had a documented side effect, allergy, or treatment failure with a preferred doxycycline/minocycline. If a product has an AB rated generic, the trial must be the generic formulation.

Public Comment: None at this time

Board Decision: The Board unanimously approved the above recommendations.

- Antivirals/Oral/Herpes Simplex Virus

  Recommendation:
    - Remove Zovirax® (acyclovir) tablets, capsules, and suspension. They are no longer available.
            - Clinical criteria:
        - Update Acyclovir suspension (age > 12 yrs), patient has a medical necessity for a non- solid oral dosage form.

- Antivirals/Oral/Influenza Medications

  Recommendation:
    - Remove age limitation on Xofluza criteria.
    - Move Relenza® (zanamivir) to non-preferred.

- Clinical criteria:
    - Add Relenza: There is a clinical, patient-specific reason the patient cannot use oseltamivir.
    - Update Xofluza: There is a clinical, patient-specific reason the patient cannot use oseltamivir.

- Cytomegalovirus (CMV) Infection Medications

Recommendation:

- Update clinical criteria for Prevymis
    - Clinical criteria: Prophylaxis of cytomegalovirus (CMV) infection in adult CMV-seropositive recipients [R+] of an allogenic hematopoietic stem cell transplant: Therapy is initiated between day 0 and day 28 post-transplantation AND therapy will continue through day 100 post-transplantation (In patients at risk for late CMV infection and disease, Prevymis may be continued through Day 200 post-HSCT) AND for approval of injection, the patient must be unable to take oral medications.
    - Prophylaxis of CMV disease in adult kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-]): Therapy is initiated between day 0 and day 7 post-transplantation AND therapy will continue through day 200 post-transplantation AND for approval of injection, the patient must be unable to take oral medications. AND the patient has a documented side effect, allergy, or contraindication to valganciclovir.

Public Comment: None at this time

Board Decision: The Board unanimously approved the above recommendations.

- Antivirals/Topical (New Drug Ycanth™ (cantharidin) Included in TCR)

Cantharidin, the active ingredient of Ycanth™, is a vesicant for topical administration. The mechanism of action for its approved indication is not known. It is indicated for the topical treatment of molluscum contagiosum in adult and pediatric patients 2 years of age and older. The safety and efficacy of Ycanth™ were assessed in two double-blind, placebo-controlled trials. The primary efficacy endpoint was the proportion of patients achieving complete clearance of all treated molluscum contagiosum lesions by day 84. Results suggest that more in the Ycanth™ group as compared with placebo achieved complete clearance (46% vs 18%, respectively, in Trial 1; 54% vs 13%, respectively, in Trial 2). Per the full-text study by Eichenfield et al, the differences between Ycanth™ and vehicle in both trials were statistically significantly different, in favor of Ycanth™ ($p<0.001$ for both studies).

Recommendation:

- Move Docosanol 10% Cream to preferred.
- Move Zovirax® (acyclovir) 5% Cream to non-preferred.

- Add Penciclovir 1% Cream and Ycanth™ (cantharidin) 0.7% Solution to non-preferred.
  - Clinical criteria:
    - Add Ycanth: The patient has a diagnosis of Molluscum Contagiosum AND either cryotherapy or curettage has failed to alleviate severe symptoms AND documentation must be submitted to support continued need if treatment duration exceeds 12 weeks.
    - Update Denavir, Penciclovir, Xerese: The patient has a treatment failure with a preferred topical acyclovir product AND for approval of penciclovir, the patient has a documented intolerance to brand Denavir.

Public Comment: None at this time

Board Decision: The Board unanimously approved the above recommendations.

- Skeletal Muscle Relaxants

Recommendation:
- Add Cyclobenzaprine ER (compare to Amrix®) with QTY LIMIT: 1 capsule/day to non-preferred.
- Remove Carisoprodol/ASA/codeine tablets and Skelaxin® (metaxalone) tablets from the PDL. They have been discontinued.
- Move Tizanidine (compare to Zanaflex®) capsules to preferred.

Public Comment: None at this time

Board Decision: A member of the Board discussed the pharmacokinetic difference between tizanidine capsules and tablets, they recommended keeping the capsules non-preferred to avoid confusion with patient dosing. The board unanimously approved the above recommendations, with the recommendation to leave tizanidine capsules as non-preferred.

- Antiretrovirals

Recommendation:
- Add Maraviroc (compare to Selzentry®) to non-preferred.
  - Clinical criteria: Maraviroc, Selzentry: The patient has been started and stabilized on the requested medication. (Note: samples are not considered adequate justification for stabilization.) OR The prescriber must provide a clinically compelling reason for the use of the requested medication including reasons why any of the preferred products would not be suitable alternatives. AND for approval of Maraviroc, the patient must have had a documented intolerance to Selzentry.
- Move Etravirine (compare to Intelence®) to preferred.
- Move Intelence® (etravirine) to non-preferred.

- Clinical criteria: Intelence: patient must have a documented intolerance to etravirine.

- Remove Lexiva® (fosemprenavir), Combivir® (lamivudine/zidovudine), Epzicom® (abacavir/lamivudine), Trizivir® (abacavir/lamivudine/zidovudine), Ziagen® (abacavir sulfate) tablet, Invirase® (saquinavir mesylate), Stavudine, Sustiva® (efavirenz), and Viramune® ER (nevirapine ER). They have been discontinued.

Public Comment: Alain Nguyen, Pharm.D, of Gilead Sciences yielded time back to the committee.

Board Decision: The Board unanimously approved the above recommendations.

Review of Newly-Developed/Revised Criteria

- None at this time

General Announcements

- FDA warns of rare but serious drug reaction to the antiseizure medicines levetiracetam (Keppra, Keppra XR, Elepsia XR, Spritam) and clobazam (Onfi, Sympazan)
  https://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-warns-rare-serious-drug-reaction-antiseizure-medicines-levetiracetam-keppra-keppra-xr-elepsia-xr

Adjourn **9:15 pm**