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

September 12, 2024: 6:00 – 8:30 p.m.

Board Members Present:

	Andy Miller, RPH		**Anne Daly, PharmD**		**Douglas Franzoni, PharmD**
	Rima Carlson, MD		**Bram Starr, MD**		**Louise Rosales, APRN**
	Katharina Cahill, PharmD				

Board Members Absent:

DVHA Staff Present:

	Stacey Baker		**Lisa Hurteau, PharmD**		**Carrie Germaine**
	Taylor Robichaud, PharmD		**Michael Rapaport, MD**		

Change Healthcare Staff Present:

	Upasana Bhatnager, MD		**Mike Ouellette, RPh**		**Molly Trayah, PharmD**

Guests/Members of the Public: Greg Kitchens, John Addelman, Folger Tuggle, Shari Orbach, Nicole Pinkerton, Scott R Ebersol, Kristen Chopas, Sandra Baldinger, Brent Fushimi, Brett Stephenson, Susanna Bachle, Erin Booth, Melissa Abbott, Timothy McSherry, Bill Eicholzer, Adam Denman, Susan Donnelly, Amy Cunningham, Nikhil Kacker, Annie Vong, Nick Trombold, Terry Dettling, Emma Booth, Kevin Gaffney, Emma Fernandez, Megan Walsh, Joe Ward

Executive Session

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

Introductions

- Attendance was called and introductions to DVHA and Change Healthcare/Optum staff were made.

DVHA Pharmacy Administration Updates: Lisa Hurteau, PharmD

- As a reminder, effective August 7, 2024, Vermont Medicaid reimplemented prior authorizations on pharmacy claims.
- The Vermont Medicaid program has proposed to discontinue coverage of over-the-counter COVID-19 self-diagnostic antigen tests in the pharmacy benefit, effective October 1, 2024. Coverage will remain in place for COVID-19 tests administered by Medicaid enrolled providers in a medical provider's office, clinic, or as inpatient or outpatient hospital services.

DVHA Chief Medical Officer Update: **Michael Rapaport, MD**

- Announcement of the new DVHA Commissioner, DaShawn Groves. He will likely attend the next DURB meeting

Follow-up Items from Previous Meetings

- None at this time.

RetroDUR/Pro DUR: Michael Ouellette, RPH, Optum

- **Introduce: The effect of Trikafta on the cost and quality of care of patients with cystic fibrosis**

Cystic fibrosis (CF) is a debilitating progressive, hereditary disease which causes progressive pulmonary decline resulting in untimely death. Mutations in the CF transmembrane conductance regulator (CFTR) protein can lead to impaired sodium and potassium transport across cell membranes resulting in high viscosity sputum, dehydration and impaired sputum clearance. CFTR modulator drugs have substantially decelerated disease progression, however recurrent respiratory infections and hospitalizations are still a reality for most patients. Until recently, available CFTR modulators included lumacaftor and tezacaftor. Ivacaftor (Kalydeco) is a chloride channel opener, also used to manage disease in combination with a CFTR and is approved for those ages 1 month and older. Lumacaftor/ivacaftor (Orkambi) is approved for those 1 year and older and tezacaftor/ivacaftor (Symdeko) is approved for those 6 years of age and older. The newest medication, Trikafta, is a combination of three drugs, two CFTR modulars (elexacaftor, tezacaftor) and ivacaftor and is considered a breakthrough in therapy for those who have at least one F508del mutation and for those with any other CFTR gene mutation that is responsive, based on in vitro and/or clinical trial data. Approximately 92% of people with CF in the US have a CFTR genotype that would qualify for this treatment once they are 2 years of age. Studies have shown significant benefits in improvements in FEV1, sweat chloride measurements and even significant improvements in patients with advanced disease. The costs of CF therapeutics can be significant and newer treatments, including Trikafta, come with substantially increased drug prices. However, the increased cost of CF drugs may be offset by decreases in other medical expenses, mainly hospital admissions.

Change Healthcare/Optum 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 Trikafta, medical and pharmacy claims will be analyzed, looking at the number and cost of hospitalizations, emergency room visits and provider visits for the year prior to and 1 year after starting the medication. For those who have initiated Trikafta for CF, this analysis will calculate if the increased cost of the drug is offset by decreased utilization of medical care.

Recommendation: None at this time.

Public Comment: None at this time.

Board Decision: None needed.

Consent Agenda Items

- **Approval of June DUR Board Minutes**
- **Biosimilar Drug Reviews**
  - Abrilada™ (adalimumab-afzb)
- **Therapeutic Drug Classes – Periodic Review**
  - Allergen Extract Immunotherapy
  - Cystic Fibrosis
  - Genital Warts
  - Iron Chelating Agents
  - NSAIDs
  - Otic Antibiotics
  - Topical Analgesics/Anesthetics
- **Review of Newly Developed/Revised Criteria**
  - Syfovre (pegcetacoplan)
  - Eylea HD (aflibercept)
  - Paxlovid (nirmatrelvir/ritonavir)

Recommendation:

- Move Eylea® HD (aflibercept) to preferred.
- Syfovre® (pegcetacoplan) QTY LIMIT: 15mg (0.1mL) per dose (each affected eye) every 25 days
  - Update Syfovre: Medication is being used for the treatment of Geographic Atrophy (GA) secondary to age-related macular degeneration (AMD) and the patient is not considered legally blind (visual acuity score of 20/200 or worse). Initial approval will be granted for 6 months. For re-approval, documentation is required showing patient has not progressed to or beyond a visual acuity score of 20/200
- Add Paxlovid® (nirmatrelvir/ritonavir) tablets to preferred.

Board Decision: The Board unanimously approved the above recommendations.

<u>Review of Newly Developed/Revised Criteria</u>

- RSV Prevention

  Recommendation:
  - Clinical criteria:
    - Update **Synagis**: If infant is in their first RSV season, the healthcare provider must provide clinical reasoning as to why infant cannot receive Beyfortus NOTE: Beyfortus is managed through the Vaccines for Children (VFC) program.
      - If infant is 8-19 months old AND entering their second RSV season AND has ONE of the following risk factors:
        - Chronic lung disease of prematurity who required medical support any time during the 6-month period before the start of the second RSV season.
        - Severely immunocompromised children

- Children with cystic fibrosis who have either manifestation or severe lung disease OR weight for length < 10th percentile
- American Indian or Alaska Native children

Provider must provide clinical reasoning why they cannot receive a second dose of Beyfortus

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

Clinical Update: Drug Reviews

Full New Drug Reviews

- Agamree® (vamorolone)

Vamorolone, the active ingredient of Agamree®, is a corticosteroid. It acts through the glucocorticoid receptor to exert anti-inflammatory and immunosuppressive effects. The exact mechanism by which vamorolone exerts its effect in patients with Duchenne muscular dystrophy is not known. It is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older. The efficacy of Agamree® for the treatment of DMD was assessed in a multicenter, randomized, double-blind, parallel-group, placebo- and active-controlled study of 24 weeks in duration which included male patients (N=121) with DMD. There is some evidence to suggest that Agamree® may be safer than prednisone when used as treatment for males with DMD in a phase 3 efficacy trial; however, there is no evidence at this time to support that Agamree® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation:

- Add Agamree® (vamorolone) suspension to non-preferred.
- Add deflazacort to non-preferred.
  - Clinical criteria:
    - Update Emflaza, Agamree, deflazacort: The patient must be ≥ 2 years of age AND The patient must have a diagnosis of Duchenne Muscular Dystrophy AND There is documented improvement in muscle function or strength with use of prednisone, but the patient has experienced weight gain >10% of body weight within 3 months or >25% within 1 year. For Agamree or deflazacort, the patient must have tried and failed or been intolerant to preferred therapies (Emflaza)

Public Comment: None at this time

Board Decision: The Board unanimously approved the above recommendations.

- Alvaiz™ (eltrombopag)

Eltrombopag, the active ingredient of Alvaiz™, is a small molecule thrombopoietin (TPO) receptor agonist for oral administration. It interacts with the transmembrane domain of the human TPO-receptor (also known as cMpl) and initiates signaling cascades that induce

proliferation and differentiation of megakaryocytes leading to increased platelet production. It is indicated for the treatment of thrombocytopenia in patients with persistent or chronic immune thrombocytopenia: for the treatment of thrombocytopenia in adults and pediatric patients 6 years and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Alvaiz™ should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding. Treatment of thrombocytopenia in patients with hepatitis C infection: for the treatment of thrombocytopenia in adult patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. It should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy. Treatment of severe aplastic anemia: for the treatment of adult patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy. Limitations of use include: Alvaiz™ is not indicated for the treatment of patients with myelodysplastic syndromes (MDS). The safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection. The effectiveness of Alvaiz™ has been established based on adequate and well-controlled studies of eltrombopag olamine in adult and pediatric patients 6 years and older with persistent or chronic ITP, adult patients with chronic hepatitis C-associated thrombocytopenia, and adult patients with refractory severe aplastic anemia. The studies included in the Alvaiz™ prescribing information (eltrombopag choline) were the same studies as in the Promacta® prescribing information (eltrombopag olamine).

Recommendation:

- Add Alvaiz™ (eltrombopag) to non-preferred.
  - Clinical criteria:
    - Update Alvaiz, Promacta: For Alvaiz (all indications) there is clinical reasoning for the inability to use preferred agents (Promacta)
      - Indication for use is chronic immune thrombocytopenia (ITP): The patient's platelet count is less than 30,000/µL (< 30 x 109/L) or the patient is actively bleeding, AND the patient has had an insufficient response or documented intolerance to corticosteroids, immunoglobulins, or splenectomy. Note: For Alvaiz, the patient must be at least 6 years old
      - Indication for use is chronic Hepatitis-C associated thrombocytopenia: The patient is at least 18 years of age AND medication is used to initiate or maintain interferon-based therapy.
      - Indication for use is Severe Aplastic Anemia: patient has had an inadequate response to standard immunosuppressive therapy (e.g. cyclosporine).

Public Comment: None at this time.

Board Discussion: A Board member asked about clarification on the requirement of splenectomy for approval of Alvaiz or Promacta. Optum provided clarification around qualifying criteria of intolerance to corticosteroids, immunoglobulins or splenectomy.

They highlighted this was an OR situation, patients are not required to have splenectomy to qualify for medication.

Board Decision: The Board unanimously approved the above recommendations.

- Filsuvez ® (birch triterpenese)

Filsuvez® topical gel is a sterile botanical drug product that contains birch triterpenes in an oil base. Birch triterpenes is a botanical drug substance composed of a mixture of pentacyclic triterpenes. The mechanism of action for its approved indication is not known. It is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older. The efficacy of Filsuvez® for the treatment of partial-thickness wounds associated with inherited EB was assessed in a randomized, double-blind, placebo-controlled study (EASE) that included adults and pediatric patients 6 months of age and older with dystrophic EB (DEB) and junctional EB (JEB). Results suggested that more in the Filsuvez® group obtained first complete closure of target wound within 45 days compared with the placebo group (NNT 9). This topical gel offers providers a treatment option for patients with either DEB or JEB.

Recommendation:

- Add Filsuvez® (birch triterpenese) gel to non-preferred.
  - Clinical criteria:
    - Add **Filsuvez:**
      - The patient has a diagnosis of dystrophic or junctional epidermolysis bullosa AND
      - The patient is at least 6 months old AND
      - The patient does not have current evidence or history of squamous cell carcinoma or active infection in the area requiring Filsuvez application AND
      - The patient has used standard wound care treatments, including silicone or foam dressings without wound resolution
      - AND 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
    - Update **Vyjuvek**: The patient has used standard wound care treatments, including silicone or foam dressings without wound resolution AND has tried and failed Filsuvez

Public Comment: None at this time.

Board Discussion: A board member asked about the duration of time that standard of care is needed before eligibility for Filsuvez. Optum explained that it would be up to the provider to determine.

Board Decision: The Board unanimously approved the above recommendations.

- Jylamvo® (methotrexate)

Methotrexate, the active ingredient of Jylamvo®, inhibits dihydrofolic acid reductase.

Dihydrofolates must be reduced to tetrahydrofolates by this enzyme before they can be utilized as carriers of one-carbon groups in the synthesis of purine nucleotides and thymidylate. Thus, methotrexate interferes with DNA synthesis, repair, and cellular replication. The mechanism of action in RA and psoriasis is not known. It is indicated for the treatment of adults: with neoplastic diseases. With acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen. With mycosis fungoides (cutaneous T-cell lymphoma) as a single agent or as part of a combination chemotherapy regimen. With relapsed or refractory non-Hodgkin lymphomas as part of a metronomic combination chemotherapy regimen. With rheumatoid arthritis (RA). With severe psoriasis. There were no clinical trials included in the Jylamvo® prescribing information. Methotrexate tablets, oral solution in a different dose, and injectable methotrexate have been available for many years and have the same indications as Jylamvo®.

Recommendation:

- Add Jylamvo® (methotrexate) solution to non-preferred.
  - Clinical criteria:
    - Update **Jylamvo, Xatmep:** The patient has a diagnosis consistent with the FDA indication of the requested drug AND patient has a requirement for an oral liquid dosage form (i.e. swallowing disorder, inability to take oral medications)

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Opsynvi® (macitentan/tadalafil)

Opsynvi® is a single tablet combination containing two oral components used to treat pulmonary arterial hypertension (PAH), including macitentan (an endothelin receptor antagonist [ERA]) and tadalafil (a phosphodiesterase 5 [PDE5] inhibitor). It is indicated for the chronic treatment of adults with pulmonary arterial hypertension (PAH, WHO Group I and WHO Functional Class (FC) II-III). The safety and efficacy of Opsynvi® were assessed in a multinational, multicenter, double-blind, adaptive, randomized, active-controlled, parallel-group study that included patients (N=187) with PAH (WHO FC II-III). The study was designed to compare the safety and efficacy of Opsynvi® to each monotherapy macitentan or tadalafil. Results suggested that Opsynvi® demonstrated greater reduction in PVR after 16 weeks. Treatment with Opsynvi® resulted in a statistically significant treatment effect of 0.71 ($p<0.0001$) representing a 29% reduction in PVR as compared to macitentan and of 0.72 ($p<0.0001$) representing a 28% reduction in PVR as compared to tadalafil. Opsynvi® is the first FDA approved once-daily single-tablet combination treatment for PAH. There is some evidence at this time from a phase 3 study to suggest that Opsynvi® may be more effective than each of its individual ingredients as monotherapy (macitentan and tadalafil) for the primary endpoint of change from baseline in PVR; however, there is no evidence at this time to support that Opsynvi® is safer or more effective than the other currently preferred, more cost-effective medications, including using the combination of macitentan and tadalafil.

Recommendation:

- Add Opsynvi® (macitentan/tadalafil) to non-preferred.
  - Clinical criteria:
    - Update **Opsumit, Opsynvi:** Patient has a diagnosis of PAH with NYHA Functional Class II or III AND Patient is not pregnant AND

Female patients have been enrolled in the REMS Program AND the patient has a documented side effect, allergy, or treatment failure with bosentan or ambrisentan. Additional criteria for Opsynvi: the patient is unable to tolerate the individual ingredient medications.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Rezdiffra™ (resmetirom)

Resmetirom, the active ingredient of Rezdiffra™, is a thyroid hormone receptor-beta agonist. It is a partial agonist of the thyroid hormone receptor-beta (THR-β). Resmetirom produced 83.8% of the maximum response compared to triiodothyronine (T3). THR-β is the major form of THR in the liver, and stimulation of THR-β in the liver reduces intrahepatic triglycerides, whereas actions of thyroid hormone outside the liver, including in heart and bone, are largely mediated through THR-α. It is indicated in conjunction with diet and exercise for the treatment of adults with non-cirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). This indication is approved under accelerated approval based on improvement of NASH and fibrosis. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Limitations of use include to avoid use of Rezdiffra™ in patients with decompensated cirrhosis. The efficacy of Rezdiffra™ was assessed based on an efficacy analysis at month 12 in Trial 1, a 54- month, randomized, double-blind, placebo-controlled trial. Results suggested that both the 80mg and 100mg dosages of Rezdiffra™ demonstrated improvement on these histopathology endpoints at month 12 compared to placebo. Furthermore, in a statistical analysis incorporating both pathologists' independent readings, Rezdiffra™ achieved statistical significance on both histopathology endpoints for both doses. Rezdiffra™ is the first FDA approved, once-daily treatment for adults with NASH with liver fibrosis.

Recommendation:

- Add Rezdiffra™ (restmetirom) to non-preferred.
  - Clinical criteria:
    - Add **Rezdiffra:** The patient must have a diagnosis of nonalcoholic steatohepatitis (NASH) with a fibrosis stage of F2 or F3 (clinical documentation provided) and a NAFLD Activity Score (NAS) of at least 4 AND the patient does not have evidence of decompensated cirrhosis.
      - Prescribed by or in consultation with Gastroenterologist or Hepatologist.
      - For Reauthorization: Documentation provided indicates positive clinical response to therapy (improvement in or stabilization of fibrosis or resolution of NASH) AND the patient has not progressed to stage F4 (cirrhosis)

Public Comment: Shari Orbach from Madrigal Pharmaceuticals highlighted the attributes of Rezdiffra.

Board Discussion: A board member explained the course of diagnosis and how NASH is being diagnosed in primary care setting more frequently using non-invasive testing and discussions questioned whether requiring biopsy for diagnosis is appropriate. A board member explained how patients would likely be referred to a specialist, who may or may not complete a biopsy. The board felt initial approval for Rezdiffra should match criteria for which the drug was studied, which included biopsy for diagnosis for NASH. The DVHA CMO explained that use will be monitored and if providers feel that biopsy is unnecessary in many cases, the criteria can be altered.

Board Decision: The Board unanimously approved the above recommendations.

- Rivfloza® (nedosiran)

Nedosiran, the active ingredient of Rivfloza®, is a double-stranded small interfering RNA (siRNA) with four covalently attached N-acetyl-D-galactosamine (GalNAc) residues. After subcutaneous administration, the GalNAc-conjugated sugars bind to asialoglycoprotein receptors (ASGPR) to deliver nedosiran to hepatocytes. It is indicated to lower urinary oxalate levels in children 9 years of age and older and adults with primary hyperoxaluria type 1 (PH1) and relatively preserved kidney function (e.g., eGFR ≥30ml/min/1.73m^2). The efficacy of Rivfloza® was assessed in a randomized, double-blind study (PHYOX2) that compared Rivfloza® and placebo in patients aged 6 years or older with PH1 or PH2 and an eGFR ≥30ml/min/1.73m^2. Too few PH2 patients were enrolled to assess efficacy in the PH2 population. Thus, Rivfloza® is only indicated for patients with PH1. Unless otherwise noted, data are presented for the complete study population (PH1 and PH2). The primary endpoint was the area under the curve, from days 90 to 180, of the percent change from baseline in 24-hour urinary oxalate excretion (AUC24-hour Uox), and Rivfloza® was significantly more effective than placebo for the primary endpoint. Rivfloza® offers providers and patients an at-home treatment option that may be self-administered or administered by a caregiver.

Recommendation:

- Add Rivfloza® (nedosiran) to non-preferred.
  - Clinical criteria:
    - Update **Oxlumo, Rivfloza:** The patient has a diagnosis of Primary Hyperoxaluria Type I (PH1) confirmed via genetic testing (identification of alanine: glyoxylate aminotransferase gene (AGXT) mutation) AND urinary oxalate excretion > 0.5mmol/1.73 m^2 or urinary oxalate: creatinine ratio is above the upper limit of normal for age AND medication is being prescribed by, or in consultation, with a nephrologist or urologist AND patient has not previously received a liver transplant. **For approval of Rivfloza**: patient must be at least 9 years of age and have a relatively preserved kidney function (eGFR ≥30ml/min/1.73m^2).

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Vevye® (cyclosporine)

Cyclosporine, the active ingredient of Vevye®, is a calcineurin inhibitor. It is a relatively selective immunomodulatory drug. It is indicated for the treatment of the signs and symptoms of dry eye disease. The safety and efficacy of Vevye® were assessed in a total of

1,369 patients with dry eye disease, of which 738 received Vevye®. In two multicenter, randomized, adequate and well-controlled studies, patients with dry eye disease were treated with Vevye® or vehicle. At day 29, there was a statistically significant higher percentage of eyes with increases of ≥10mm from baseline in Schirmer's wetting with Vevye® as compared with vehicle (NNT 13 study 1, NNT 26 study 2). There are other cyclosporine ophthalmic products available that are also indicated for dry eye disease, including Cequa® (solution 0.9mg/ml, 0.09%) and Restasis® (emulsion 0.05%). Vevye® is the only water-free cyclosporine dissolved in a semi fluorinated alkane, for dry eye disease. Per the manufacturer, this product spreads uniformly over the ocular surface. This product offers prescribers another treatment option.

Recommendation:

- Add Vevye® (cyclosporine) ophthalmic solution to non-preferred.
  - Clinical criteria:
    - Update **Cequa, Vevye:** The patient has a diagnosis of Dry Eye Disease AND has a documented side effect, allergy, or treatment failure to two ophthalmic immunomodulators, one of which must be Restasis. **For approval of Vevye:** the patient must have had a treatment failure with Cequa.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Voydeya™ (danicopan)

Danicopan, the active ingredient of Voydeya™, is a small molecule complement Factor D inhibitor. It binds reversibly to complement Factor D and selectively inhibits the alternative complement pathway. Danicopan prevents the cleavage of complement Factor B into the Ba and Bb fragments, which are required for the formation of the alternative pathway (AP) complement component C3 convertase (C3bBb), the generation of downstream effectors including C3 fragment opsonization, and the amplification of the terminal pathway. It is indicated as an add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH). A limitation of use includes that Voydeya™ has not been shown to be effective as monotherapy and should only be prescribed as an add-on to ravulizumab or eculizumab. The safety and efficacy of Voydeya™ were assessed in adults with PNH and clinically significant EVH in a multiple-region, randomized, double-blind, placebo-controlled study. The primary outcome measure was the change in Hgb level from baseline to week 12. Efficacy was established based on the demonstration of superiority of Voydeya™ in combination with ravulizumab or eculizumab compared to placebo in combination with ravulizumab or eculizumab in all efficacy measures, with statistically significant results.

Recommendation:

- Add Voydeya™ (danicopan) to non-preferred.
  - Clinical criteria:
    - Add **Voydeya:** The patient has a diagnosis of extravascular hemolysis (EVH) with paroxysmal nocturnal hemoglobinuria (PNH) AND there has been disease progression despite being on a stable dose of ravulizumab or eculizumab AND the patient will remain on ravulizumab or eculizumab (only approved as add-on

therapy) Note: Requires provider to be enrolled in REMS program

Public Comment: Terry Dettling from AstraZeneca highlighted the attributes of Voydeya.

Board Discussion: A board member asked about Voydeya being limited distribution (for example some drugs are only dispensed by Onco360 pharmacy), would this be a barrier to patients obtaining access. DVHA administration reviewed this is a relatively common process, and the pharmacy would enroll with Vermont Medicaid.

Board Decision: The Board unanimously approved the above recommendations.

- Wainua™ (eplontersen)

Eplontersen, the active ingredient of Wainua™, is a transthyretin-directed antisense oligonucleotide (ASO), covalently linked to a ligand containing three N-acetyl galactosamine (GalNAc) residues to enable delivery of the ASO to hepatocytes. It is an antisense oligonucleotide-GalNAc conjugate that causes degradation of mutant and wild-type transthyretin (TTR) mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues. It is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. The efficacy of Wainua™ was demonstrated in a randomized, open-label, multicenter trial that included adults with polyneuropathy caused by hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis; Study 1). Results suggested that treatment with Wainua™ resulted in statistically significant improvements in the mNIS+7 and the Norfolk QoL-DN total scores compared to the external placebo control (both $p<0.001$) at week 35. Wainua™ provides another treatment option for polyneuropathy of hereditary transthyretin-mediated amyloidosis, which can be administered by the patient once monthly and has no box warning.

Recommendation:

- Add Wainua™ (eplontersen) to non-preferred.
  - Clinical Criteria:
    - Add Wainua to Amvuttra, Onpattro, Tegsedi criteria
- Remove Tegsedi as no longer available as of 9/27/24

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Winrevair™ (sotatercept- csrk)

Sotatercept-csrk, the active ingredient of Winrevair™, is a homodimeric recombinant fusion protein consisting of the extracellular domain of the human activin receptor type IIA (ActRIIA) linked to the human IgG1 Fc domain. Sotatercept-csrk, a recombinant activin receptor type IIA-Fc (ActRIIA-Fc) fusion p rotein, is an activin signaling inhibitor that binds to activin A and other TGF-β superfamily ligands. As a result, sotatercept-csrk improves the balance between the pro-proliferative and anti-proliferative signaling to modulate vascular proliferation. In animal models of PAH, a sotatercept-csrk analog reduced inflammation and inhibited proliferation of endothelial and smooth muscle cells in diseased vasculature. These cellular changes were associated with thinner vessel walls, partial reversal of right ventricular remodeling, and improved hemodynamics. It is indicated for the treatment of adults with

pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group 1) to increase exercise capacity, improve WHO functional class (FC), and reduce the risk of clinical worsening events. The efficacy of Winrevair™ was assessed in adult patients with PAH in the STELLAR study, a global, multicenter, double-blind, placebo-controlled, parallel-group clinical trial. The primary endpoint was the change from baseline at week 24 in 6MWD. In the Winrevair™ group, the placebo-adjusted median increase in 6MWD was 41 meters ($p<0.001$). The number of subjects who experienced death or at least one clinical worsening event was significantly less in the Winrevair™ group as compared with placebo ($p<0.001$; NNT 5). Winrevair™ is a first-in-class treatment for PAH WHO Group 1. There is some evidence at this time to suggest that Winrevair™ plus background therapy is more effective than placebo plus background therapy for the primary endpoint of change in 6-minute walk distance; however, there is no evidence at this time to support that Winrevair® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation:

- Add Winrevair™ (sotatercept-csrk) to non-preferred.
  - Clinical criteria:
    - Add **Winrevair:** The patient has a diagnosis of pulmonary arterial hypertension (PAH) Group 1 and WHO functional class II or III AND
      - The patient must have a LV end diastolic pressure of ≤ 15 mmHg AND
      - The patient must be on stable doses of standard of care therapy (patient-specific dose goal for each PAH therapy achieved) AND
      - The patient has a 6MWT between 150-500 meters AND
      - The patient has used dual combination therapy from two other PAH-indicated drug classes, unless contraindicated, for at least 60 days and has experienced continued decline in pulmonary hemodynamics and exercise capacity

Public Comment: Sandra Baldinger from Merck highlighted the attributes of Winrevair.

Board Decision: The Board unanimously approved the above recommendations.

- Zilbrysq® (zilucoplan)

Zilucoplan, the active ingredient of Zilbrysq®, is a complement inhibitor. It binds to the complement protein C5 and inhibits its cleavage to C5a and C5b, preventing the generation of the terminal complement complex, C5b-9. The exact mechanism of action of zilucoplan for its approved indication is not known but it is presumed to involve reduction of C5b-9 deposition at the neuromuscular junction. It is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. The efficacy of Zilbrysq® for the treatment of gMG in adults who are anti-AChR antibody positive was established in a 12-week, multicenter, randomized, double-blind, placebo-controlled study. At week 12, treatment with Zilbrysq® demonstrated a statistically significant improvement from baseline compared to placebo for MG-ADL total score (primary endpoint) and QMG total score. Zilbrysq® is the first FDA-approved once-daily subcutaneous treatment for adults with gMG who are anti-AChR antibody-positive that may be self-administered.

Recommendation:

- Add Zilbrysq® (zilucoplan) to non-preferred.
  - Clinical criteria:
    - Add Zilbrysq: The 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 ≥6 at baseline 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.
    - 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 or QMG score.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Zituvio™ (sitagliptin)

Sitagliptin free base, the active ingredient of Zituvio™, is a dipeptidyl peptidase-4 (DPP-4) inhibitor, which is thought to exert its actions in patients with type 2 DM by slowing the inactivation of incretin hormones. Concentrations of the active intact hormones are increased by sitagliptin, thus increasing and prolonging the action of these hormones. Incretin hormones (including glucagon-like peptide-1 [GLP-1] and glucose-dependent insulinotropic polypeptide [GIP]) are released by the intestine and levels are increased in response to a meal. These hormones are rapidly inactivated by the enzyme, DPP-4. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (DM). There were about 5200 patients with type 2 DM randomized in 9 double-blind, placebo-controlled clinical safety and efficacy trials conducted to evaluate the effectiveness of sitagliptin on glycemic control. The studies found in the Zituvio™ prescribing information were the same as those found in the Januvia® prescribing information, which is a brand name for sitagliptin that has been available for several years. There were no new efficacy studies found in the Zituvio™ prescribing information, but rather they were the same studies found in the Januvia® tablets (sitagliptin) prescribing information supporting safety and efficacy of sitagliptin as compared with placebo and as compared with other active comparators. Januvia® has been available for several years and proven to be an effective treatment for type 2 DM.

Recommendation:

- Add Zituvio™ (sitagliptin) to non-preferred.
  - Clinical criteria:
    - Add Zituvio to Alogliptan criteria.
- Remove Onglyza® (saxagliptin) from the PDL as no longer available

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Zoryve foam® (roflumilast)

Roflumilast, the active ingredient of Zoryve®, and its active metabolite (roflumilast N-oxide) are inhibitors of phosphodiesterase 4 (PDE4). Roflumilast and roflumilast N-oxide inhibition of PDE4 (a major cyclic 3'5'-adenosine monophosphate [cyclic AMP] metabolizing enzyme) activity leads to accumulation of intracellular cyclic AMP. The specific mechanism(s) by which roflumilast exerts its therapeutic action is not well defined. It is indicated for the treatment of seborrheic dermatitis in adult and pediatric patients 9 years of age and older. The efficacy of Zoryve® foam was assessed in two randomized, double-blind, vehicle-controlled trials that included adult and pediatric subjects (N=683 total) with seborrheic dermatitis involving the scalp, face, and/or body with an Investigator Global Assessment (IGA) of moderate or severe (IGA of 3 or 4 on a 5-point scale from 0-4). In each trial, subjects were randomized to receive Zoryve® foam or vehicle foam applied once daily for 8 weeks. The primary endpoint was the proportion of subjects who achieved IGA treatment success at week 8, with success being defined as a score of 'clear' (0) or 'almost clear' (1), plus a 2-grade improvement from baseline. More in the Zoryve® foam group achieved IGA success as compared with the vehicle foam. Per the full-text study (STRATUM) by Blauvelt et al[2], the results for IGA success were statistically significantly in favor of Zoryve® foam ($p<0.001$). Head-to-head studies with other active ingredients were not found.

Recommendation:

- Add Zoryve® (roflumilast) foam to non-preferred
  - Update clinical criteria **Zoryve**: the patient has a diagnosis consistent with the FDA indication of the requested formulation AND has had an inadequate response (defined as daily treatment for at least one month), adverse reaction, or contraindication to at least 2 different preferred agents for that diagnosis

Public Comment: Brett Stephenson from Arcutis Biotherapeutics highlighted the attributes of Zoryve.

Board Decision: The Board unanimously approved the above recommendations.

New Managed Therapeutic Drug Classes

- None at this time

Therapeutic Drug Classes – Periodic Review

- Acne

- Cabtreo® (clindamycin phosphate/benzoyl peroxide/adapalene gel)

Cabtreo® is a combination product that contains clindamycin (a lincosamide antibacterial), adapalene (binds to specific retinoic acid nuclear receptors; a modulator of cellular differentiation, keratinization, and inflammatory processes) and benzoyl peroxide (an oxidizing agent with bactericidal and keratolytic effects). It is indicated for the topical treatment of acne vulgaris in adult and pediatric patients 12 years of age and older. The

efficacy of Cabtreo® was assessed in two multicenter, randomized, double-blind clinical trials (Trial 1 and Trial 2) in adult and pediatric subjects 10 years of age and older (N=363) with facial acne vulgaris. Note that while subjects aged 10 to less than 12 years of age were included in these trials, Cabtreo® is not approved for use in patients less than 12 years of age. he co-primary efficacy endpoints of success on the EGSS, absolute change in non-inflammatory lesion count, and absolute change in inflammatory lesion count were assessed at week 12. More achieved success on the EGSS in the Cabtreo® group vs the vehicle group, while also having a greater mean percent reduction and mean absolute reduction in both non-inflammatory and inflammatory facial lesions. In addition, Cabtreo® also resulted in significantly greater reductions in inflammatory/non-inflammatory lesions as compared with vehicle ($p<0.001$ for all). Cabtreo® is the first triple-combination gel FDA approved for acne vulgaris.

Recommendation:

- Add Cabtreo® (clindamycin phosphate/benzoyl peroxide/adapalene gel) to non-preferred.
    - Clinical criteria:
        - Add Cabtreo: Patient must try and have failed individual preferred products
- Add Finacea 15% Foam to preferred.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Phosphate Binders

    - Xphozah® (tenapanor)

Tenapanor, the active ingredient of Xphozah®, is a locally acting inhibitor that targets the sodium/hydrogen exchanger 3 (NHE3), an antiporter expressed on the apical surface of the epithelium of the small intestine and colon. Inhibition of NHE3 by tenapanor results in reduced sodium absorption and decreased phosphate absorption by reducing phosphate permeability through the paracellular pathway. It is indicated to reduce serum phosphorus in adults with chronic kidney disease (CKD) on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy. The efficacy of Xphozah® for the ability to lower serum phosphorus in adults with CKD on dialysis was assessed in 3 trials, including TEN-02-201, TEN-02-301, and TEN-02-202. Data from the two phase 3 monotherapy studies suggested that during the randomized withdrawal period, phosphorus levels significantly rose in the placebo group relative to patients who remained on Xphozah®.There is some evidence in a phase 3 study to suggest that Xphozah® in combination with phosphate binder may be more effective for lowering serum phosphorus compared to placebo plus phosphate binder; however, there is no evidence at this time to support that Xphozah® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation:

- Add Xphozah® (tenapanor) to non-preferred.
    - Clinical criteria:
        - Add Xphozah: The patient must have a documented side effect, allergy, or inadequate response to two non-calcium- containing

binders (sevelamer, lanthanum, ferric citrate, and sucroferric oxyhydroxide)

Public Comment: None at this time

Board Decision: The Board unanimously approved the above recommendations.

- Substance Use Disorder Treatments

  - Rextovy® (naloxone spray)

Naloxone, the active ingredient of Rextovy®, is an opioid antagonist. It antagonizes opioid effects by competing for the same receptor sites. Naloxone reverses the effects of opioids, including respiratory depression, sedation, and hypotension. It can also reverse the psychotomimetic and dysphoric effects of agonist-antagonists such as pentazocine. It is indicated for emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression, for adult and pediatric patients. Rextovy® nasal spray is intended for immediate administration as emergency therapy in settings where opioids may be present. It is not a substitute for emergency medical care. It is intended for immediate administration as emergency therapy in settings where opioids may be present, and it is not a substitute for emergency medical care. No new clinical trials were found for this product, but this offers providers and patients another treatment option.

Recommendation:

- Add Rextovy® (naloxone HCl) nasal spray to non-preferred.
  - Clinical criteria:
    - Add Rextovy to Opvee and Zimhi criteria.

Public Comment: None at this time

Board Decision: The Board unanimously approved the above recommendations.

General Announcements

- None at this time.

Adjourn **7:55 pm**