Department of Vermont Health Access
Pharmacy Benefit Management Program

DUR Board Meeting Minutes
May 9, 2017

Board Members:

Present:
Zail Berry, MD  Clayton English, PharmD  Louise Rosales, NP
Renee Mosier, PharmD  Jocelyn VanOpdorp, PharmD
Patricia King, MD

Absent: Bill Breen, RPh  Alisson Richards, MD

Staff:
Laurie Brady, RPh, ChangeHealthCare  MaryBeth Bizzari, RPH, DVHA  Stacey Baker, DVHA
Jacquelyn Hedlund, MD, ChangeHealthcare  Jennifer Egelhof, DVHA  Jason Pope, DVHA
Michael Ouellette, RPh, ChangeHealthCare  Scott Strenio, MD, DVHA

Guests:
Thomas Algozzine, Novo Nordisk  Kristen Chopas, Gilead  Adam Denman, Otsuka
Christine Dube, MedImmune  Margaret Glassman, Alkermes  James Kokoszyna, Allergan
John Meyer, Otsuka  Jeffrey Olson, Gilead  Scott Williams, J & J
Jessica Kritzman, Abbott  Patrick Lievano, Abbott  Folger Tuggle, Bioverativ
Jane Guio, Otsuka  James Minnucci, Genentech

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

2. Introductions and Approval of DUR Board Minutes:
   - Introductions were made around the table.
   - The April meeting minutes were accepted as printed.

3. DVHA Pharmacy Administration Updates: Mary Beth Bizzari, RPh, DVHA
   - None at this time
4. Medical Director Update: Dr. Scott Strenio, DVHA
   - Welcome back to Dr. Strenio
   - No other updates at this time.

5. Follow-up Items from Previous Meetings: Laurie Brady, RPh, Change Healthcare
   - Long-term use of Skeletal Muscle Relaxants

Skeletal muscle pain is a frequent complaint in clinical practice. Numerous treatment options exist, including topical agents, NSAIDs, antidepressants, anticonvulsants, anesthetic and steroid injections, DMARDs and muscle relaxants. Generally, muscle relaxants should be used for 2-3 weeks to treat acute pain, per guidelines and the prescribing information provided by the drug manufacturers. Muscle relaxants have strong anticholinergic properties and can have the unwanted side effects of dizziness, fatigue and impaired cognition. In addition, they have addictive properties and lose effectiveness over time. They generally are not recommended for use in the elderly population and there are many possible drug-drug interactions and side effects that make them potentially dangerous. We proposed to examine the use of skeletal muscle relaxants among Vermont Medicaid members, specifically looking at members who have been prescribed the medications for longer than 30 consecutive days. We were also interested in identifying members who have been co-prescribed opioids or benzodiazepines within the same 30-day period. As follow-up to the initial analysis, we then looked at members who had prolonged treatment defined as more than 90 consecutive days within 1 year to see if there was widespread chronic usage among those prescribed muscle relaxants.

A total of 2,925 unique patients were identified as using > 90 cumulative days of a skeletal muscle relaxant therapy in a 365-day period. A total of 1,887 prescribers wrote prescriptions for these patients. 765 were prescribers of Baclofen, Tizanidine, and/or Dantrolene. 1,122 were prescribers of Carisoprodol, Chlorzoxazone, Cyclobenzaprine, Metaxalone, Methocarbamol, and/or Orphenadrine. Top diagnoses are low back pain, major depressive disorder, lumbago, other chronic pain, anxiety disorder, backache and cervicalgia. Broken down by product cyclobenzaprine has the majority and over all higher use in female patient’s verses male.

Considerations for action are: Consider quantity limits per month for these medications (e.g. 12 tabs per 30 days). Determine appropriate criteria for the continuation of muscle relaxants beyond duration limitations set, given appropriate usage is short-term per PI and professional society guidelines. Consider a general education strategy for all VT
prescribers, as there is widespread prescription of these drugs in the medical community.

**Board Decision:** The Board decided that putting quantity limit in place, refill limitations, and/or diagnosis exclusions would be good but given the complexity and number of patients affected would like to bring this back to the next meeting. Also, bring back a draft educational letter to send out to providers.

6. RetroDUR/DUR: Laurie Brady, RPh, Change Healthcare and Jacquelyn Hedlund, MD, Change Healthcare

- **Introduce: Second Generation Antipsychotics in the Treatment of Major Depressive Disorder**

  Major Depressive Disorder (MDD), also called unipolar depression or non-psychotic depression, is a serious and widespread illness in the general population. Estimates are that in 2015, 16.1 million adults over the age of 18 had at least one major depressive episode, equating to 6.7% of that population. In 2009-2010, 8 million adult ambulatory visits in the US had MDD as the primary diagnosis. While some episodes of depression are of limited duration and not recurrent, many people who suffer from depression will have episodes of long duration and will relapse.

  Our proposal is to investigate medical management of members with MDD. We are interested in looking at the number of members on a single antidepressant, combination of antidepressants or a combination of antidepressant(s) and atypical antipsychotic medications. Specifically, we are interested in identifying members with MDD diagnosis who are being treated or maintained on an atypical (second generation) antipsychotic medication alone, without an antidepressant, which is not a practice supported by guidelines.

  We will use paid, non-reversed Medicaid pharmacy and medical claims data for calendar year 2016, excluding members with Part D, VMAP and Healthy Vermonters coverage. We will identify members with diagnoses of major depressive disorder excluding those with diagnoses of bipolar disorder, schizophrenia or schizoaffective disorder. Of those members, we will identify how many are taking antidepressant medications (one or two) and how many are taking adjunctive antipsychotic medications or antipsychotic medications alone.

**Board Decision:** The board would like to look at medication use in MDD with and without psychotic features (comparing data between the two). Another consideration is to look at dosing as low doses are sometimes used a for sleep. The board would also like to add in the diagnosis of OCD, however, that may outside the scope of the intended focus on Major Depressive Disorder.
Data presentation: Adherence to Guidelines for Monitoring DMARD’s

Conventional (non-biologic) disease modifying anti-rheumatic drugs (DMARDs) are used to treat a variety of rheumatologic conditions. The goals of using these immunosuppressant medications are: induce or maintain a remission; reduce the incidence of disease flares or relapse; and allow a reduction in the use of glucocorticoids while controlling disease. The DMARDs work in several ways. Some are cytotoxic, and some inhibit steps in the pathway that promotes inflammation. Still others work by inhibiting lymphocyte production or function. All of these drugs have the potential to cause significant toxicity and use must be monitored carefully. The traditional DMARDs are methotrexate (hepatic, renal and hematologic toxicity), hydroxychloroquine (ocular toxicity), sulfasalazine (hematologic toxicity) and leflunomide (hematologic, hepatic and renal toxicity). While not considered traditional DMARDs, the non-biologic drugs cyclosporine and mycophenolate (hepatic, renal, hematologic, vascular toxicity) and azathioprine (hematologic, hepatic toxicity) will be considered here too since the use of these drugs is not uncommon.

We identified members who were prescribed one of the DMARDs (methotrexate, sulfasalazine, hydroxychloroquine, leflunomide, azathioprine, cyclosporine, mycophenolate). We then examined medical claims to document measurement of CBCs, LFTs and creatinine at least once in members on all medications except hydroxychloroquine. For members on hydroxychloroquine, we looked to see that at least one eye exam was done while the member was taking the drug.

Results illustrate that the vast majority of patients on DMARD therapy (excluding hydroxychloroquine) are having labs drawn as recommended. Total distinct member count 980 of those 86% with all labs done, 9% with partial labs done and 6% with no labs done. The distinct member count for Hydroxychloroquine is 560. Of those patients, 52% had an eye exam within the 2 year time frame analyzed and 48% did not have an eye exam in their medical records during that time. These numbers illustrate that there may be a gap in care for those on hydroxychloroquine. Targeted provider outreach could be considered for prescribers of this medication.

Board Decision: Concern was discussed that patients may not have access to eye exams. Dr. Stenio will research optometrists and ophthalmologists that accept VT Medicaid. A targeted mailing will then be sent out to rheumatologists regarding the recommendation for a yearly eye exam in members on hydroxychloroquine. We could also reach out to blue print groups to educate them that an eye exam is needed.
7. Review of Newly-Developed/Revised Clinical Coverage Criteria and/or Preferred Products:

- None at this time.

**Board Decision:** None needed.


**Abbreviated New Drug Reviews:**
- None at this time.

**Full New Drug Reviews:**

a) **Bromsite®** (bromfenac ophthalmic solution)

- Bromfenac, the active ingredient of Bromsite®, is a nonsteroidal anti-inflammatory drug (NSAID). Its mechanism of action is thought to be due to its ability to block prostaglandin synthesis by inhibiting cyclooxygenase 1 and 2. Bromsite® is a sterile aqueous topical NSAID formulated in DuraSite® for ophthalmic use. It is indicated for the treatment of post-operative inflammation and prevention of ocular pain in patients undergoing cataract surgery. Bromsite® should be administered at least 5 minutes after instillation of other topical medications. It may be administered in conjunction with other topical ophthalmic medications, such as alpha-agonists, beta-blockers, carbonic anhydrase inhibitors, cycloplegics, and mydriatics.

**Public Comment:** No public comment.

**Recommendation:**
- Add Bromsite® to non-preferred.
- Remove Bromday from the PDL and criteria no longer available.
- Clinical criteria:
  - Add Bromsite to the Acular LS, Bromfenac, Diclofenac, Ocupen and Prolensa criteria.

**Board Decision:** The Board unanimously approved the above recommendation.

b) **Vemlidy®** (tenofovir alafenamide)

- Included in the Therapeutic Class Review (TCR).
Recommendation: PDL placement and criteria will be recommended when the TCR is reviewed.

Board Decision: Defer decision- to occur with the class review.

c) Rayaldee® (calcifediol)

- Included in the Therapeutic Class Review (TCR).

Recommendation: PDL placement and criteria will be recommended when the TCR is reviewed.

Public Comment: No public comment.

Board Decision: Defer decision- to occur with the class review.

9. Therapeutic Drug Classes – Periodic Review: Jacquelyn Hedlund, MD, Change Healthcare and Laurie Brady, RPh, Change Healthcare

a) Hepatitis B

- Hepatitis viruses are associated with striking morbidity and mortality worldwide, including acute hepatic decompensation, cirrhosis, and hepatocellular carcinoma (HCC). In the United States, the rate of new hepatitis B virus (HBV) infections has declined by about 82% since 1991, with 3,050 new cases of acute HBV reported to the CDC in 2013. Nevertheless, the actual number of new infections is higher as many are either asymptomatic or were never reported (an estimated 19,764 persons newly infected with HBV in 2013). An estimated 240 million people are infected chronically with HBV worldwide, while approximately 700,000-1.4 million people are chronically infected in the United States.

- When choosing an antiviral therapy several factors must be considered: safety, efficacy, risk of resistance, cost, and pregnancy status. Lamivudine (Epivir®) has been shown to be inferior to entecavir and telbivudine in randomized clinical trials. Telbivudine is associated with a moderate rate of resistance unless serum HBV DNA levels are undetectable at week 24, although as a pregnancy category B drug it has a role in preventing vertical transmission of HBV in HBeAg-positive pregnant women. This leaves IFN, entecavir (Baraclude®) or tenofovir (Viread®) as recommended first line treatments for most patients. Patients with minimal disease and those who are unlikely to achieve sustained response should not be treated with NAs, especially when they are less than 30 years of age. Peginterferon alfa-2a is a reasonable first line treatment in patients with genotype A or B who are young, lack significant co-morbidities and have HBV DNA levels < 10^9 copies/ml and ALT levels ≥ 2-3 x ULN. Entecavir is recommended for children older than 2 years of age, as is lamivudine. In
patients with confirmed or suspected antiviral resistance to lamivudine, entecavir, adefovir, or telbivudine, a switch to tenofovir is recommended. Other considerations will include prior treatments, if any; coinfection with HIV and concurrent or planned anti-retroviral therapy. It is vital to stress the importance of compliance in order to minimize the risk of resistance.

- Tenofovir alafenamide fumarate, the active ingredient of Vemlidy®, is an antiviral drug active against the hepatitis B virus (HBV). Tenofovir alafenamide is a prodrug of tenofovir, which is converted to tenofovir through hydrolysis. Tenofovir is subsequently phosphorylated to the pharmacologically active metabolite tenofovir diphosphate. Tenofovir diphosphate inhibits HBV replication through incorporation into viral DNA by the HBV reverse transcriptase, which results in DNA chain-termination. Tenofovir alafenamide fumarate (Vemlidy®) was FDA approved in 2016 and has been shown to have similar efficacy to tenofovir disoproxil but a potentially better adverse event profile.

**Recommendation:**

- Add a Hepatitis B Agents therapeutic category to the PDL with current users grandfathered.
- Add Entecavir and Viread® to preferred.
- Add Adefovir, Baraclude®, Epivir-HBV®, Hepsera®, Lamivudine HBV, Vemlidy® to non-preferred.
- Clinical criteria:
  - Adefovir, Hepsera, Lamivudine HBV, Epivir-HBV: The prescriber must provide 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 brand Hepsera or Epivir-HBV, the patient has a documented intolerance to the generic. Note: AASLD and WHO guideline recommend these not be utilized first line due to potential for the development of resistance.
  - Baraclude tabs: the patient has a documented intolerance to generic entecavir.
  - Baraclude suspension: the patient has a medical necessity for a non-solid oral dosage form
  - Vemlidy: the patient must have documented bone loss, renal insufficiency (CrCl < 30ml/min), or other contraindication to Viread.

**Public Comment:** Jeffery Olson, Gilead; Highlighted attributes of Vemlidy.

**Board Decision:** The Board unanimously approved the above recommendation with the modification of Vemlidy criteria to: the patient has a diagnosis of osteoporosis, renal insufficiency (CrCl < 60ml/min), or other contraindication to Viread such as chronic corticosteroid use.
b) **Alpha-1 Proteinase Inhibitor**
   - Alpha-1 antitrypsin (AAT) deficiency is a genetically linked enzyme disorder that affects the lungs, liver, and rarely, skin. In the lungs, it results in slow, progressive destruction of pulmonary function, as AAT deficiency causes chronic obstructive pulmonary disease (COPD). AAT inactivates the enzyme neutrophil elastase (NE) in the lung tissue, with elastase destroying elastin and AAT protecting against the degradation of elastin. AAT deficiency is characterized by a plasma level of AAT below the believed protective threshold of 11 μM. Because of the deficiency, unopposed neutrophil elastase (NE) in the lung tissue results in the gradual destruction of lung causing early onset emphysema. Furthermore, cigarette smoking and infection increases elastase production in the lung. While generally thought to be rare, there are approximately 80,000-100,000 people in the U.S. that have severe deficiency of AAT. It is likely to go unrecognized and underdiagnosed.
   - A 2016 Cochrane Review by Gotzsche et al included 3 randomized controlled trials (N=283) to assess the safety and efficacy of augmentation with IV alpha-1 antitrypsin in those with alpha-1 antitrypsin deficiency and lung disease. There were more exacerbations in the treatment group as compared with placebo; however, statistically there was the possibility of no true difference. The reported quality of life was similar between treatment groups. Forced expiratory volume in one second (FEV1) worsened more in those from the active treatment group as compared with placebo, but was not significantly different. The authors concluded that due to sparse data, a conclusion about the impact augmentation therapy has on various outcomes could not be made.

**Recommendation:** No changes at this time.

**Public Comment:** No public comment.

**Board Decision:** The Board unanimously approved the above recommendation.

c) **Contraceptive Products**
   - Per a 2016 study by Finer et al, 45% of pregnancies in 2011 were unintended.
   - Implanon® is no longer active or rebatable and so has been removed from the class review.
   - No significant changes.

**Recommendation:**

**Biphasic**
   - Add Bekyree and Kimidess to preferred.
   - Add Azurette and Lo Loestrin FE to non-preferred.
Emergency Contraceptive Agents
   - Add Option2, React, and Fallback Solo to preferred.
   - Remove Plan B One step from the PDL.

Extended Cycle
   - Move Amethia, Ashlyna, Daysee and Quartette to non-preferred.

Injectable Agents
   - No changes

Long-Acting Reversible Contraceptives (LARC’s)
   - Add Liletta IUD, Mirena IUD, Skyla IUD, and Nexplanon Implant to preferred.
   - Add Kyleena IUD to non-preferred.
   - Clinical criteria:
       - The prescriber must provide a clinically valid reason for the use of the requested medication including reasons why any of the preferred products would not be a suitable alternative.

Monophasic Agents
   - Add Blisovi FE 24, Drospirenone/Ethinyl Estradiol/Levomefol, Junel FE 24, Microgestin FE, Rajani, Tayulla, and Zenchent FE to non-preferred.
   - Remove LoEstrin, Lo/Ovral 21, Lo/Ovral 28, Modicon, Nordette 28, and Ortho Cept 28 from the PDL as they are either non-rebateable or no longer available.

Progestin Only Contraceptives
   - Remove Norlyroc and Nor QD from the PDL as they are no longer rebatable.

Topical Agents
   - Remove Ortho Evra Patch from the PDL as it is no longer rebateable.

Triphasic
   - Move Ortho Tri Cyclen Lo to non-preferred.

Vaginal Ring
   - No changes at this time.

Public Comment: No public comment.
Board Decision: The Board unanimously approved the above recommendation.

d) Prenatal Vitamins
   - No new drugs.
   - No significant changes.
   - A 2016 systematic review and meta-analysis by Vahdaninia et al included 5 randomized controlled trials to assess the effect of vitamin interventions during pregnancy on developing allergic diseases in offspring. The authors concluded that the current evidence suggests that prenatal supplementation of vitamin D may have a beneficial effect on recurrent wheezing in children but that longer-term studies are needed.

Recommendation:
   - Add Citranatal Harmony, Citranatal 90 DHA, Citranatal B-CALM, Citranatal RX, Citranatal Assure, Citranatal DHA, Concept OB, and Concept DHA to preferred.
   - Remove Prenate AM Tab, Prenate Cap Enhance, Prenate Cap Essential, Prenate Cap Restore, Prenate DHA Cap, Prenate Mini Cap, Virt-IRT- PN DHA Cap, Virt-PN Plus Cap from the preferred side of the PDL. They will be now non-preferred.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

e) Platelet Aggregation Inhibitors
   - No new drugs.
   - Anti-platelet therapy is a complex therapeutic area with rapidly evolving data. Fortunately, there are well-respected, evidence-based, multi-society guidelines that can help direct the most appropriate therapy. Many nuances of therapy, particularly with the P2Y agents are based on the details of the clinical situation and patient characteristics and are discussed in detail in these guidelines. The guidelines provide recommendations on both the choice of agent as well as the duration of therapy.
   - Brilinta and Effient are showing in studies that they are very effective drugs used in combination with aspirin in patients who have acute coronary syndromes with or without stenting stents. In fact, the data is looking like they may have better efficacy then Plavix.

Recommendation:
Remove Pletal and Persantine from the PDL as they are no longer available.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

f) Parathyroid Agents
- Hyperparathyroidism (HPT) results from the proliferation of the chief cells that secrete excess parathyroid hormone (PTH) from one or more of the four parathyroid glands. Parathyroid hormone helps the body regulate calcium homeostasis. When the parathyroid glands detect low or falling serum calcium concentration, PTH is released. This mobilizes calcium from the bones, causes the kidneys to reabsorb calcium, and stimulates GI absorption of calcium by converting 25-hydroxyvitamin D3 to the active form, 1,25 dihydroxyvitamin D3. Over-secretion of PTH, however, results in hypercalcemia.
- Calcifediol (Rayaldee®) is synthetically manufactured as calcifediol monohydrate and is a prohormone of the active form of vitamin D3, calcitriol. Calcifediol is converted to calcitriol by CYP27B1, also called 1-alpha hydroxylase. Calcitriol binds to the vitamin D receptor in target tissues and activates vitamin D responsive pathways that result in increased intestinal absorption of calcium and phosphorus and reduced parathyroid hormone synthesis. Calcifediol is also known as calcidiol, 25-hydroxycholecalciderol, or 25-hydroxyvitamin D3. The manufacturer recommends monitoring serum calcium, serum phosphorus, serum total 25-hydroxyvitamin D and intact PTH levels at a minimum of 3 months after starting therapy or dose adjustment, and subsequently at least every 6 to 12 months with calcifediol (Rayaldee®). Prior to raising the dose, ensure serum calcium is below 9.8mg/dl, serum phosphorus is below 5.5mg/dl, and serum total 25-hydroxyvitamin D is below 100ng/ml.

Recommendation:
- Add Rayaldee to non-preferred.
- Clinical criteria:
  - Non-preferred agents (except Natpara): The patient must have a documented side effect, allergy, or treatment failure to two preferred agents. If a product has an AB rated generic, one trial must be the generic formulation.

Public Comment: No public comment.
**Board Decision:** The Board unanimously approved the above recommendation.

### 10. Newly Developed/Revised Criteria: Laurie Brady, RPh, Change Healthcare

- **Actinic Keratosis Therapy**
  - Move Aldara 5% cream to non-preferred.
  - Move Imiquimod 5% cream to preferred and remove clinical criteria.
  - **Clinical criteria:**
    - Add Aldara: the patient has a documented intolerance to generic imiquimod.
    - Revise Picato: The diagnosis or indication is actinic keratosis AND The patient has had a documented side effect, allergy, contraindication or treatment failure with a generic topical fluorouracil product AND The patient has had a documented side effect, allergy, contraindication or treatment failure with generic imiquimod.

- **Non-biologic Psoriasis Agents (oral)**
  - Move Acitretin to preferred and remove the clinical criteria.
  - Move Soriatane to non-preferred.
  - **Clinical criteria:**
    - Add Soriatine: the patient has a documented intolerance to generic acitretin capsules.

- **Beta-adrenergic Agents: Short-acting nebulizer solutions**
  - Remove different strengths of Albuterol (2.5mg, 5mg, and .63mg) and list as all strengths on the PDL.
  - Move levalbuterol neb sol (age ≤ 12yrs) to preferred.
  - Move Xopenex to non-preferred (regardless of age).
  - Add age > 12 yrs to levalbuterol neb sol on non-preferred side of PDL.
  - **Clinical criteria:**
    - Revise Levalbuterol, Xopenex nebulizer solution (age > 12 years): The patient must have had a documented side effect, allergy, or treatment failure to albuterol nebulizer AND for approval of brand Xopenex, the patient must have had a documented intolerance to the generic.

### 11. General Announcements:

**Selected FDA Safety Alerts**

FDA alerts consumers of nationwide voluntary recall of EpiPen and EpiPen Jr

FDA approves two hepatitis C drugs for pediatric patients
https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm551407.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Information on Erythropoiesis-Stimulating Agents (ESA) Epoetin alfa (marketed as Procrit, Epogen), Darbepoetin alfa (marketed as Aranesp)

FDA Drug Safety Communication: FDA restricts use of prescription codeine pain and cough medicines and tramadol pain medicines in children; recommends against use in breastfeeding women

12. Adjourn: Meeting adjourned at 8:05 p.m.