Department of Vermont Health Access
Pharmacy Benefit Management Program
**DUR Board Meeting Minutes**
May 10, 2022

**Board Members Present:**

Mark Pasanen, MD
Bill Breen, RPH
Douglas Franzoni, PharmD
Claudia Berger, MD,
Lucy Miller, MD
Andy Miller, RPH
Renee Mosier, PharmD

**Absent:** Joseph Nasca, MD, Margot Kagan, PharmD

**Staff:**

Laurie Brady, RPh, Change HealthCare
Marietta Scholten, DVHA
Jason Pope, DVHA
Lisa Hurteau, PharmD, DVHA
Sandi Hoffman, DVHA
Carrie Germaine, DVHA
Jacquelyn Hedlund, MD, Change Healthcare
Mike Ouellette, RPh, Change Healthcare

**Guests:**

Adam Denman (Global Blood Therapeutics)
Kristen Chopas (Gilead)
Rasheed Jandali
John E. Davis
Lisa Libera
Rasheed Jandali
Mariola Vazquezv (Leo Pharma)
Mark Golick (Neurocrine)
Matt Nguyen (Abbvie)
Lindsey Walter
Megan Walsh (Abbvie)
Paul Isikwev (Teva)
John Ciruso
Nikhil Kradker (Genetech)
Frank Lamotte (GSK)
Nicolas Primpas

**1. Executive Session:**

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

**2. Introductions and Approval of DUR Board Minutes:**

- Attendance was called and introductions of DVHA and Change Healthcare staff were made.
- The April meeting minutes were accepted as printed.

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

- Lisa has officially stepped into Nancy Hogue's former role as the DVHA Pharmacy Director. DVHA has a requisition to backfill the Clinical Pharmacist role.

**4. Medical Director Update: Marietta Scholten, MD, DVHA**

- Dr. Logan was unable to start as the medical director, and the position is now open again.

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

- None at this time.

**7. RetroDUR/ProDUR: Jacqueline Hedlund, MD, Change Healthcare and Mike Ouellette, MD, Change Healthcare**

- Data presentation: Use of Letrozole in Female Members

Letrozole, an aromatase inhibitor with brand name Femara®, has indications for treatment in hormone receptor positive breast cancer, in the adjuvant, extended adjuvant, and advanced disease settings. The oral dosing in all these settings is 2.5 mg daily. In breast cancer, off-label indications include using in combination with other drugs in the advanced disease and metastatic settings, again at 2.5mg/day dosing. Other off-label indications include treatment of recurrent ovarian cancer (2.5mg/day) and infertility/ovulation stimulation in anovulatory females with polycystic ovarian syndrome. The doses in this case include 2.5 up to 7.5mg/day, starting day 3-5 of the cycle for 5 days. It is important to note that not all anovulatory treatment is done to treat infertility. For example, causes of anovulation include polycystic ovary syndrome, hypogonadatropic hypogonadism, primary ovarian insufficiency, and hyperprolactinemia. It is established that anovulatory or oligo-ovulatory women are at higher risk of endometrial cancers and regulating the menstrual cycle is desirable. Treatment of infertility is not a covered benefit in members who receive Medicaid drug coverage in Vermont, therefore the decision was made to evaluate the use of letrozole in women of child-bearing age in this population.

Change Healthcare used paid, non-reversed Medicaid pharmacy and medical claims from SFY 2021 excluding members with Part D, VMAP and Healthy Vermonters coverage. They identified women between the ages of 20 and 50 who were taking letrozole and identify the ordering provider to determine whether the medication may have been prescribed for fertility. It appears possible that many, if not most, women being prescribed letrozole were taking it to improve the odds of getting pregnant, as most were younger women who were prescribed letrozole for 5 or fewer days. Most of the prescribers were OB/GYN providers, or providers who practiced both Endocrinology and OB/GYN. There were a few members (5) with a breast cancer diagnosis and a few members were on continuous therapy, supporting a diagnosis other than fertility, however that was not the majority of claims. Letrozole is not expensive, however its use for treatment of infertility is not consistent with Medicaid policy.

**Recommendation:** A reminder to OB/GYN and Endocrinology providers of the policy could help prevent inappropriate Medicaid billing. Additionally, a Prior Authorization on letrozole for patients under the age of 50 may be an effective way to ensure compliance with the policy prohibiting Medicaid from covering drugs for treating infertility.

*Public Comment:* No public comment.

**Board Decision:** The Board unanimously approved the above recommendation along with the implementation of Auto PA for those with a cancer diagnosis on file.

- Introduction: Use of Opioids from Multiple Providers

Monitoring of opioid prescribing has been a focus of federal and state medical agencies for several years. Prescription monitoring systems have been instituted, and prescribers must query the database before writing an opioid prescription for a patient when such a prescription exceeds 10 pills. Per the Vermont Prescription Monitoring System (VPMS) Rule, "The intent is to promote public health through enhanced opportunities to prevent, detect and treat misuse of controlled substances, without interfering with the legitimate medical use of those substances." Pharmacies are required to report all controlled substance dispensing, and Vermont-licensed pharmacists are required to query the VPMS in the following circumstances:
1.) Prior to dispensing a prescription for a Schedule II, III, or IV opioid controlled substance to a patient who is new to the pharmacy.
2.) When an individual pays cash for a prescription for a Schedule II, III, or IV opioid controlled substance and the individual has prescription drug coverage on file.
3.) When a patient requests a refill of a prescription for a Schedule II, III, or IV opioid controlled substance substantially in advance of when a refill would ordinarily be due; and
4.) When the dispenser is aware that the patient is being prescribed Schedule II, III, or IV opioid controlled substances by more than one prescriber.

The database includes information about the prescriber, the dispensing pharmacy, the payment methods (including cash) and the dates, names and doses of the opioids prescribed. It is important that providers utilize the system to be sure that members are not getting multiple prescriptions of opioids inappropriately. In theory, this tracking should minimize provider shopping to get opioids beyond what has been prescribed by one provider. Additionally, credentialing and quality assessment agencies, such as HEDIS, are using opioid prescribing and monitoring to measure quality and these ratings are being used by payers and the public alike. Of note, the use of VPMS in treating patients in hospice care, and other end-of-life care is not required.
Change Healthcare will use paid, non-reversed Medicaid pharmacy claims from calendar year 2021, excluding members with Part D, VMAP and Healthy Vermonters coverage. They will identify all adult members receiving prescriptions for opioids from four or more different prescribers during the year. The analysis will only include prescriptions billed through Vermont Medicaid. It will not include cash prescriptions. For those with multiple prescribers, they will look to see if there was dose escalation and if any of the prescriptions overlapped.

**Recommendation:** None at this time.

*Public Comment:* No public comment.

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

**8. Clinical Update: Drug Reviews: Jacquelyn Hedlund, Change Healthcare and Laurie Brady RPh, Change Healthcare**

**Biosimilar Drug Reviews:**

- Releuko™ (filgrastim-ayow) will be discussed as part of the Therapeutic Class Review.

**Full New Drug Reviews:**

- Livmarli® (maralixibat)

Maralixibat, the active ingredient of Livmarli®, is a reversible inhibitor of the ileal bile acid transporter (IBAT). It decreases the reabsorption of bile acids (primarily the salt forms) from the terminal ileum. Pruritus is a common symptom in patients with Alagille syndrome (ALGS) and the pathophysiology of pruritus in patients with ALGS is not completely understood. While the complete mechanism by which maralixibat improves pruritus in ALGS patients is not known, it may involve inhibition of the IBAT, which results in decreased reuptake of bile salts, as observed by a decrease in serum bile acids. It is indicated for the treatment of cholestatic pruritus in patients with ALGS 1 year of age and older. Serum fat-soluble vitamin (FSV) levels should be obtained at baseline and monitored during treatment, along with any clinical manifestations. If FSV deficiency is diagnosed, supplement with FSV. The safety and efficacy of Livmarli® were assessed in Trial 1, which consisted of an 18-week, open-label treatment period; a 4-week randomized, double-blind, placebo-controlled, drug-withdrawal period; a subsequent 26-week, open-label treatment period; and a long-term open-label extension period. In one small study that included pediatric ALGS patients with cholestasis and pruritus, on average, patients administered Livmarli® for 22 weeks maintained pruritus reduction whereas those in the placebo group who were withdrawn from Livmarli® after 18 weeks returned to baseline pruritus scores by week 22.

**Recommendation:**

- Add Livmarli® (maralixibat) to non-preferred.
  - Clinical criteria:
    - Add Livmarli: The patient is experiencing moderate to severe pruritis associated with a diagnosis of Alagille Syndrome (ALGS) AND baseline liver function tests and fat-soluble vitamin (A, D, E, and K) levels have been completed and will be monitored periodically during treatment AND patient has had an inadequate response or contraindication to cholestyramine and ursodiol. For re-approval, there must be documented clinical improvement (e.g. reduced serum bile acid or decreased pruritis).

*Public Comment:* No public comment.

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

- Skytrofa® (lonapegsomatropin-tcgd)

Lonapegsomatropin-tcgd, the active ingredient of Skytrofa®, is a long-acting prodrug of a human growth hormone (somatropin) produced by recombinant DNA technology using E. coli.

It is a pegylated human growth hormone (somatropin). Somatropin binds to the growth hormone (GH) receptor in the cell membrane of target cells resulting in intracellular signal transduction and a host of pharmacodynamic effects. It has direct tissue and metabolic effects, and indirect effects mediated by insulin-like growth factor-1 (IGF-1), including stimulation of chondrocyte differentiation and proliferation, stimulation of hepatic glucose output, protein synthesis, and lipolysis. It is indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH). The safety and efficacy of Skytrofa® were assessed in a multicenter, randomized, open-label, active-controlled, parallel-group phase 3 study that was conducted in treatment-naïve, prepubertal pediatric subjects with growth hormone deficiency (GHD). The primary efficacy endpoint was annualized height velocity at week 52. Results suggested that treatment with once-weekly Skytrofa® for 52 weeks resulted in an annualized height velocity of 11.2 cm/year. The authors noted that the treatment difference in annualized height velocity favoring Skytrofa® started at week 5 and continued to the end of the trial, becoming statistically significant from week 26 onward. In addition, there were no serious adverse events related to study drug and no adverse event led to treatment discontinuation or death. The rates of adverse events and serious adverse events were similar between groups. The authors concluded that this trial met its objective of non-inferiority in annualized height velocity and further demonstrated superiority of Skytrofa® to daily somatropin, with a similar safety profile.

**Recommendation:**

- Add Skytrofa® (lonapegsomatropin-tcgd) to non-preferred.
  - Clinical criteria:
    - Add Skytrofa to the Nutropin AQ, Omnitrope, Saizen and Zomacton clinical criteria.

*Public Comment:* No public comment.

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

- Thyquidity® (levothyroxine sodium solution)

Thyquidity® contains synthetic levothyroxine (T4) sodium. Synthetic T4 is chemically identical to that produced in the human thyroid gland and is slightly soluble in water. Thyroid hormones exert their physiologic actions through control of DNA transcription and protein synthesis. Triiodothyronine (T3) and L-thyroxine (T4) diffuse into the cell nucleus and bind to thyroid receptor proteins attached to DNA. This hormone nuclear receptor complex activates gene transcription and synthesis of messenger RNA and cytoplasmic proteins. The physiological actions of thyroid hormones are produced mainly by T3, the majority of which (about 80%) is derived from T4 by deiodination in peripheral tissues. Oral levothyroxine sodium is a synthetic T4 hormone that exerts the same physiologic effect as endogenous T4, thus maintaining normal T4 levels when a deficiency is present. It is indicated for Hypothyroidism: As a replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism. Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) Suppression: As an adjunct to surgery and radioiodine therapy in the management of

thyrotropin-dependent well-differentiated thyroid cancer. Limitations of use include: Thyquidity® is not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients as there are no clinical benefits and overtreatment with Thyquidity® may induce hyperthyroidism. Thyquidity® is not indicated for treatment of hypothyroidism during the recovery phase of subacute thyroiditis. There is no clinical trials section for Thyquidity®. Synthetic levothyroxine has been able available for many years, both as brand and generic versions. Thyquidity® is a new liquid dosage form to be administered by a calibrated oral syringe that allows for individualized dosing for patients. There is no evidence at this time to support that Thyquidity® is safer or more effective than the other currently preferred, more cost-effective medications.

**Recommendation:**

- Add Thyquidity™ (levothyroxine sodium) oral solution and Tirosint®-Sol (levothyroxine sodium) oral solution to non-preferred.
    - Clinical criteria:
        - Add Thyquidity, Tirosint-Sol: The patient has a medical necessity for a non-solid oral dosage form and the medication cannot be administered by crushing oral tablets AND for approval of Tirosint-Sol, the patient must have a documented intolerance to Thyquidity.

*Public Comment:* No public comment.

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

- Tyrvaya® (varenicline nasal spray)

Varenicline, the active ingredient of Tyrvaya®, is a partial nicotinic acetylcholine receptor agonist of several receptors and a full α7 receptor agonist. The efficacy of Tyrvaya® for its approved indication is believed to be the result of the activity of varenicline at heteromeric sub-type(s) of the nicotinic acetylcholine (nACh) receptor where its binding produces agonist activity and activates the trigeminal parasympathetic pathway resulting in increased production of basal tear film as a treatment for dry eye disease. The exact mechanism of action is not known at this time. It is indicated for the treatment of the signs and symptoms of dry eye disease. The safety and efficacy of Tyrvaya® for the treatment of dry eye disease were assessed in two randomized, multicenter, double-masked, vehicle-controlled studies (ONSET-1 and ONSET-2). In ONSET 1, patients (N=182) were randomized to receive one spray in each nostril BID of varenicline solution 0.006mg, Tyrvaya® 0.03mg, varenicline solution 0.06mg or vehicle. In ONSET-2, patients (N=758) were randomized to receive one spray in each nostril BID of Tyrvaya® 0.03mg, varenicline solution 0.06mg, or vehicle. Most included in the studies were female (74%) and had a mean age of 61 years. The mean baseline anesthetized Schirmer's score was 5.1mm and the mean baseline eye dryness score (EDS) was 59.3. Use of artificial tears was allowed during the studies. In two randomized, double-blind, vehicle-controlled studies, significantly greater proportion of patients in the Tyrvaya® group had ≥10mm increase in tear

production at day 28 as compared with vehicle in study 1 (NNT 3) and study 2 (NNT 5). Tyrvaya® offers prescribers another treatment option for dry eye disease.

**Recommendation:**

- Add Cyclosporin ophthalmic emulsion 0.05% droperette (compare to Restasis®) with QTY LIMIT: 180 vials per 90 days and Tyrvaya® (varenicline) nasal spray with QTY LIMIT: 2 bottles (8.4mL) per 30 days to non-preferred.
    - Clinical criteria:
        - Revise Cequa: 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.
        - Add Cyclosporin emulsion and Tyrvaya to the Xiidra clinical criteria.

*Public Comment:* No public comment.

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

**9. New Therapeutic Drug Classes**

- None at this time.

**10. Therapeutic Drug Classes- Periodic Review:**

- **Atopic Dermatitis (new drug Adbry® (tralokinumab-ldrm), Cibinqo® (abrocitinib) and Opzelura® (ruxolitinib) included**
    - Tralokinumab-ldrm, the active ingredient of Adbry®, is an interleukin-13 antagonist, a human IgG4 monoclonal antibody that specifically binds to human interleukin-13 (IL-13) and inhibits its interaction with the IL-13 receptor α1 and α2 subunits (IL-13Rα1 and IL-13Rα2). IL-13 is a naturally occurring cytokine of the Type 2 immune response. Tralokinumab-ldrm inhibits the bioactivity of IL-13 by blocking IL-13 interaction with IL-13Rα1/IL-4Rα receptor complex. Tralokinumab-ldrm inhibits IL-13 induced responses including the release of proinflammatory cytokines, chemokines, and IgE. It is indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Adbry® can be used with or without topical corticosteroids. The safety and efficacy of Adbry® were assessed in three double-blind, randomized, placebo-controlled trials (ECZTRA 1, ECZTRA 2, ECZTRA 3) that included adult subjects 18 years of age and older (N=1934 total) with moderate-to-severe atopic dermatitis not adequately controlled by topical medication(s). The efficacy of Adbry® was assessed

in 3 randomized, double-blind, placebo-controlled trials that compared Adbry® with placebo in adults with moderate-to-severe atopic dermatitis not adequately controlled by topical medication(s). In one study, Adbry® was used in combination with TCS and compared with placebo plus TCS and as needed topical calcineurin inhibitors. All three trials assessed the primary endpoints of the proportion of subjects with an IGA 0 or 1 at week 16 and the proportion of subjects with EASI-75 at week 16. Significant differences were also observed in the outcomes for the ECZTRA 1 and EZCTRA 2 studies.3 Direct head-to-head comparisons with other active ingredients indicated for atopic dermatitis were not identified.

- Abrocitinib, the active ingredient of Cibinqo®, is a Janus kinase (JAK) inhibitor. It reversibly inhibits JAK1 by blocking the adenosine triphosphate (ATP) binding site. In a cell-free isolated enzyme assay, abrocitinib was selective for JAK1 over JAK2, JAK3, and tyrosine kinase (TYK) 2, as well as the broader kinome. The relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known. It is indicated for the treatment of adults with refractory, moderate-to-severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable. Cibinqo® is not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants. The safety and efficacy of Cibinqo® as monotherapy and in combination with background topical corticosteroids (TCS) were assessed in 3 randomized, double-blind, placebo-controlled trials (Trial-AD-1, Trial-AD-2, and Trial-AD-3) that included subjects 12 years of age and older (N=1615) with moderate to severe atopic dermatitis as defined by the Investigator's Global Assessment (IGA) score ≥3, Eczema Area and Severity Index (EASI) score ≥16, body surface area (BSA) involvement ≥10%, and Peak Pruritus Numerical Rating Scale (PP-NRS) ≥4 at the baseline visit prior to randomization. (Note that Cibinqo® is not approved for use in pediatric patients.) There is some evidence at this time in a phase 3 study to suggest that Cibinqo® 200mg is significantly more effective than dupilumab with respect to itch response at week 2 and some evidence to suggest that Cibinqo® plus TCS is more effective than placebo plus TCS for primary endpoints of IGA response and EASI-75 response; however, there is no head-to-head evidence to suggest that it is safer or more effective than the other currently preferred, more cost-effective medications. Furthermore, the indication for Cibinqo® notes that its use is for patients not adequately controlled with other systemic drug products, including biologics (or when use of those therapies is inadvisable).
- Ruxolitinib, the active ingredient of Opzelura®, is a Janus kinase (JAK) inhibitor that inhibits JAK1 and JAK2 which mediate the signaling of a

number of cytokines and growth factors that are important for hematopoiesis and immune function. JAK signaling involves recruitment of STATs (signal transducers and activators of transcription) to cytokine receptors, activation, and subsequent localization of STATs to the nucleus leading to modulation of gene expression. The relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known. It is indication for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Use of Opzelura® in combination with therapeutic biologics, other JAK inhibitors, or potent immunosuppressants such as azathioprine or cyclosporine is not recommended. Opzelura® has a box warning regarding serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis. The safety and efficacy of Opzelura® were assessed in two double-blind, randomized, vehicle-controlled trials of identical design (Trial 1 and Trial 2) that included subjects 12 years of age and older (N=1249) with atopic dermatitis for ≥2 years. One network meta-analysis suggests that some topical JAK inhibitors, including ruxolitinib 1.5% BID, may be more effective than topical PDE4 inhibitors and tacrolimus; however, there is no head-to-head evidence at this time to support that Opzelura® is safer or more effective than the other currently preferred, more cost-effective medications.

- In January 2022, the FDA approved Rinvoq® (upadacitinib) for the treatment of moderate to severe atopic dermatitis in adults and children 12 years of age and older whose disease did not respond to previous treatment and is not well controlled with other pills or injections, including biologic medicines, or when use of other pills or injections is not recommended. RINVOQ 15 mg once daily can be initiated in adults and children 12 years of age and older weighing at least 40 kg. In these children and adults less than 65 years of age who do not achieve an adequate response, the dose may be increased to 30 mg once daily. The FDA approval is supported by efficacy and safety data from one of the largest registrational Phase 3 programs for atopic dermatitis with more than 2,500 patients evaluated across three studies. Approximately 52 percent of the patients had prior exposure to systemic atopic dermatitis treatment. These studies evaluated the efficacy and safety of RINVOQ monotherapy (Measure Up 1 and 2) and with topical corticosteroids (AD Up), compared to placebo, in adults and children 12 years of age and older with moderate to severe atopic dermatitis. Across the three atopic dermatitis pivotal studies, RINVOQ (15 mg and 30 mg, once daily) monotherapy and with topical corticosteroids met all primary and

secondary endpoints at week 16, with some patients achieving higher levels of skin clearance (EASI 90 and 100).

- The Rinvoq® drug label comes with the following Black Box Warning: • Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving Rinvoq. • If a serious infection develops, interrupt Rinvoq until the infection is controlled. • Prior to starting Rinvoq, perform a test for latent tuberculosis; if it is positive, start treatment for tuberculosis prior to starting Rinvoq. • Monitor all patients for active tuberculosis during treatment, even if the initial latent tuberculosis test is negative. • Lymphoma and other malignancies have been observed in patients treated with Rinvoq. • Thrombosis, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis, have occurred in patients treated with Janus kinase inhibitors used to treat inflammatory conditions.

**Recommendation:**

Oral Agents

- Remove Protopic® (tacrolimus) ointment from the PDL.
- Move Elidel® to preferred for ages ≥ 2, Tacrolimus 0.03% ointment to preferred for ages ≥ 2, and Tarcolimus 0.1% ointment to preferred for ages ≥ 16.
- Add Adbry® (tralokinumab-ldrm) subcutaneous injection) to preferred after clinical criteria are met with QTY LIMIT: 6 syringes the first 28 days then 4 syringes every 28 days thereafter.
- Add Cibinqo® (abrocitinib) tablets to non-preferred with QTY LIMIT: 1 tab/day; Maximum 30 days supply.
- Add Opzelura® (ruxolitinib) to non-preferred.
- Add Rinvoq® (upadactinib) extended-release tablet to non-preferred with QTY LIMIT: 1 tablet/day; Maximum 30 days supply.
    - Clinical criteria:
        - Add Opzelura: The patient is ≥ 12 years of age AND The patient has a diagnosis of mild-moderate atopic dermatitis (eczema) AND The patient has had a documented side effect, allergy, or treatment failure (defined as daily treatment for at least one month) with at least one moderate to high potency topical corticosteroid within the last 6 months, unless contraindicated AND The patient has had a documented side effect, allergy, or treatment failure (defined as daily treatment for at least one month) of a preferred topical calcineurin inhibitor and crisabarole ointment AND

Patient is not receiving Opzelura in combination with another biologic medication (e.g. dupilumab), oral JAK inhibitor (e.g. upadactinib), or systemic immunosuppressant (e.g. cyclosporine) AND The quantity requested does not exceed 60 grams/fill; maximum of 8-weeks of continuous use.

- Revise Pimecrolimus: The patient has a documented intolerance to brand Elidel.
- Revise Adbry, Cibinqo, Dupixent, Rinvoq: The patient's age is FDA approved for the given indication AND The patient has a diagnosis of moderate to severe atopic dermatitis AND The prescription is initiated in consultation with a dermatologist, allergist, or immunologist AND At least 10% of the body's surface area is involved AND The patient has had a documented side effect, allergy, or treatment failure (defined as daily treatment for at least one month) with at least one moderate to high potency topical corticosteroid and one preferred topical calcineurin inhibitor within the last 6 months AND Initial approval will be granted for 6 months. For re-approval after 6 months, the prescriber must submit documentation of clinical improvement in symptoms. Renewals may be granted for up to 1 year.
- Add Cibinqo additional criteria: The patient has a had a documented side effect, allergy, or treatment failure with Adbry or Dupixent AND the patient has a had a documented side effect, allergy, or treatment failure with Rinvoq.
- Add Rinvoq additional criteria: The patient has a had a documented side effect, allergy, or treatment failure with Adbry or Dupixent.

*Public Comments*: Mariola Vazquez from Leo Pharma: Time yielded back to the committee. Matt Nguyen from Abbvie: Highlighted the attributes of Rinvoq.

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

- **Bladder Relaxants**
  - In March 2021, the FDA approved a new indication for Myrbetriq® (mirabegron extended-release tablets) and Myrbetriq® Granules (mirabegron for extended-release oral suspension) to treat neurogenic detrusor overactivity (NDO), a bladder dysfunction related to neurological impairment, in children ages three years and older.

Myrbetriq® is also indicated for overactive bladder in adult patients. NDO is a dysfunction of the bladder that results from congenital conditions (inherited conditions beginning at or before birth), such as spina bifida, or other disease or injury in the nervous system, such as spinal cord injury. With NDO, there is overactivity of the bladder wall muscle, which normally relaxes to allow storage of urine. The bladder wall muscle overactivity in NDO results in sporadic bladder muscle contraction, which increases pressure in the bladder and decreases the volume of urine the bladder can hold. If NDO is not treated, increased pressure in the bladder can put the upper urinary tract at risk of harm, including possible permanent damage to the kidneys. In addition, spontaneous bladder muscle contractions can lead to unexpected and frequent leakage of urine with symptoms of urinary urgency (immediate need to urinate), frequency (urinating more often than normal) and incontinence (loss of bladder control).

- The efficacy of Myrbetriq® and Myrbetriq® Granules for the pediatric NDO indication was established in a study of 86 patients ages 3 to 17 years old. Improvements occurred in patients' maximum cystometric (bladder) capacity, number of detrusor (bladder wall muscle) contractions, volume of urine held until first detrusor (bladder wall muscle) contraction and number of daily urine leakage episodes after 24 weeks of treatment. The most common side effects with Myrbetriq® and Myrbetriq® Granules with NDO were urinary tract infection, nasopharyngitis (common cold), constipation and headache. Myrbetriq® and Myrbetriq® Granules may increase blood pressure and may make blood pressure worse in patients with a history of high blood pressure. Myrbetriq® and Myrbetriq® Granules may cause angioedema, an allergic reaction with swelling of the lips, face, tongue or throat. Patients should promptly discontinue Myrbetriq® and Myrbetriq®Granules and seek medical attention if angioedema associated with upper airway swelling occurs, as this may be life-threatening.
- Myrbetriq® and Myrbetriq® Granules are two different products and they are not substitutable on a milligram-per-milligram basis. For pediatric patients weighing 35kg or more with NDO, use Myrbetriq® or Myrbetriq® Granules. The recommended starting dose is Myrbetriq® 25mg QD. If needed, increase to a maximum dose of Myrbetriq® 50mg QD after 4 to 8 weeks. The recommended starting dosage of Myrbetriq® Granules is 6ml (48mg) PO QD. If needed, increase to a maximum dosage of Myrbetriq®

Granules 10ml (80mg) QD after 4 to 8 weeks. A recommended dosage for Myrbetriq® Granules for adults has not been determined.

- In June 2021, the FDA approved Pfizer's Toviaz (fesoterodine fumarate) for the treatment of neurogenic detrusor overactivity (NDO) in pediatric patients 6 years of age and older with a bodyweight greater than 25 kg. Toviaz is also approved for the treatment of overactive bladder (OAB) in adults with symptoms of urge urinary incontinence, urgency, and frequency.
- The approval of Toviaz for the new indication was based on a randomized, open-label study consisting of a 12-week efficacy phase followed by a 12-week safety extension phase in pediatric patients from 6 years to 17 years of age. During the 12-week efficacy phase, 124 patients were randomized to receive Toviaz 4 mg, Toviaz 8 mg, or active comparator orally once daily. The primary efficacy endpoint was the mean change from baseline in maximum cystometric bladder capacity (MCBC) at week 12. Treatment with Toviaz 4 mg or 8 mg daily resulted in improvements from baseline to week 12 in the primary efficacy endpoint, MCBC, for pediatric patients, with numerically higher changes from baseline for Toviaz 8 mg daily than for Toviaz 4 mg daily. The change from baseline with Toviaz 4 mg was 58.1 (95% CI: 28.8, 87.4) and with Toviaz 8 mg the change from baseline was 83.4 (95% CI: 54.2, 112.5). The most common adverse reactions (≥ 2%) with Toviaz use in pediatric patients with NDO were diarrhea, urinary tract infection, dry mouth, constipation, abdominal pain, nausea, increased weight, and headache. In pediatric patients weighing greater than 25 kg and up to 35 kg, the recommended dose of Toviaz is 4 mg orally once daily. If needed, dosage may be increased to Toviaz 8 mg orally once daily. In pediatric patients weighing greater than 35 kg, the recommended starting dosage of Toviaz is 4 mg orally once daily. After one week, the dose should be increased to 8 mg orally once daily.

**Recommendation:**

- Remove Enablex® (darifenacin) from the PDL.
- Add Myrbetriq® ER Granules for Suspension to non-preferred.
    - Clinical criteria:
        - Revise Myrbetriq Granules, Vesicare LS: The patient has a diagnosis of neurogenic detrusor overactivity AND the patient has a documented side effect, allergy, or treatment failure

with oxybutynin or Toviaz AND for patients ≥ 18 years of age, medical necessity has been provided for a liquid formulation.
    - Remove note: Patients < 21 years of age are exempt from all ORAL ANTIMUSCARINIC Urinary Antispasmodics PA requirements.

*Public Comments*: No public comment.

**Board Decision:** None needed.

- **Benign Prostatic Hyperplasia (BPH) Agents**
    - No new drugs.
    - No other significant clinical changes.

**Recommendation:**

- Remove gender and age limitations for finasteride.

*Public Comments:* No public comment.

**Board Decision:** None needed.

- **Colony Stimulating Factor (CSF) Agents (biosimilar Releuko® (filgrastim-ayow) included)**
    - In February 2022, the FDA approved Releuko™ (filgrastim-ayow), a biosimilar to Neupogen® (filgrastim). The approval was based on data demonstrating that the biosimilar product and the reference product were highly similar, and that there were no clinically meaningful differences between the 2 agents. Releuko™, a leukocyte growth factor, is approved to:
        - Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
        - Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia.
        - Reduce the duration of neutropenia and neutropenia-related clinical sequelae, eg, febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.

        - Reduce the incidence and duration of sequelae of neutropenia in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.
    - Releuko™ is supplied in single-dose vials and single-dose prefilled syringes containing 300mcg or 480mcg of filgrastim-ayow in a preservative-free solution. The product is expected to be available in the third quarter of 2022.

**Recommendation:**

- Add Releuko® (filgrastim-ayow) and Leukine® (sargramostim) to non-preferred.
    - Clinical criteria:
        - Add Releuko, to the Granix, Leukine, Nivestym, Zarxio syringe clinical criteria.

*Public Comments:* Paul Isikwe from Teva Pharmaceuticals: Highlighted the attributes of Granix.

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

- **Erythropoietin Stimulating Agents**
    - No new drugs.
    - No other significant clinical changes.

**Recommendation:**

- No changes.

*Public Comments:* No public comment.

**Board Decision:** None needed.

- **Immunosuppressants**
    - No new drugs.
        - Acute inflammatory syndrome (AIS) has been reported with the use of MMF and mycophenolate products, and some cases have resulted in hospitalization. AIS is a paradoxical pro-inflammatory reaction characterized by fever, arthralgias, arthritis, muscle pain and elevated inflammatory markers including, C-reactive protein and erythrocyte sedimentation rate, without evidence of infection or underlying disease recurrence. Symptoms occur within weeks to months of initiation of treatment or a dose increase. After discontinuation, improvement of symptoms and inflammatory markers are usually

observed within 24 to 48 hours. Monitor patients for symptoms and laboratory parameters of AIS when starting treatment with mycophenolate products or when increasing the dosage. Discontinue treatment and consider other treatment alternatives based on the risk and benefit for the patient.
    - American College of Rheumatology Guidelines suggest holding the dose of mycophenolate mofetil (MMF) for one to two weeks as disease activity allows after each COVID vaccine dose.

**Recommendation:**

- No changes.

*Public Comments:* No public comment.

**Board Decision:** None needed.

- **Idiopathic Pulmonary Fibrosis (IPF)**
    - No new drugs.
    - No other significant clinical changes.

**Recommendation:**

- No changes.

*Public Comments:* No public comment.

**Board Decision:** None needed.

- **Movement Disorder**
    - No new drugs.
    - In 2019, the Canadian Journal of Psychiatry published treatment recommendations for tardive dyskinesia.34 Results suggested that:
        - "In most patients with schizophrenia, stopping antipsychotic therapy is not an option for the treatment of TD due to the increased risk of relapse."
        - "Patients must be warned that TD symptoms may worsen transiently as medication dosages are lowered (withdrawal emergent dyskinesias)." (regarding antipsychotics)
        - "There is insufficient evidence to recommend dose reduction as a treatment for TD. Targeting the low end of the recommended dose range throughout treatment is recommended to limit the risk of developing TD." (regarding antipsychotics)

- "Switching from an FGA (first generation antipsychotic), particularly haloperidol, to an SGA (second generation antipsychotic) with a lower D2 affinity, such as clozapine or quetiapine, may be effective in reducing TD symptoms. All antipsychotic medications are associated with a risk of TD; though, the available evidence suggests that the risk may be lower with SGAs. Clinicians and patients must be aware that improvement in symptoms may take months or years to occur."
- "There is good evidence to support a favorable benefit-risk ratio for valbenazine as a treatment for TD. Valbenazine should be considered a first-line treatment for TD."
- "There is good evidence for a favorable benefit-risk ratio for deutetrabenazine as a treatment for TD. Deutetrabenazine should be considered a first-line treatment for TD."
- "There is limited evidence for the use of tetrabenazine for the treatment of TD. The current available evidence suggests that, while tetrabenazine may be helpful for TD, its use is associated with more adverse effects than valbenazine and deutetrabenazine. Given the higher-quality evidence in support of the other VMAT2 inhibitors with fewer adverse effects, valbenazine and deutetrabenazine should be preferred over tetrabenazine for the treatment of TD."

**Recommendation:**

- Move Austedo® (deutetrabenazine) tablets with QTY LIMIT: 48 mg/day; Maximum 1-month supply per fill and Ingrezza® (valbenazine tosylate) capsules with QTY LIMIT: 80 mg/day; Maximum 1-month supply per fill to preferred after clinical criteria are met.
  - Clinical criteria:
    - Revise Austedo: The diagnosis or indication for the requested medication is Huntington's Disease (HD) with chorea or Tardive Dyskinesia (TD) AND the results of an Abnormal Involuntary Movement Scale (AIMS) exam have been submitted AND the patient is ≥18 years of age. For re-approval, there must be documented clinical improvement.
    - Revise Ingrezza: The diagnosis or indication for the requested medication is Tardive Dyskinesia (TD) AND the results of an Abnormal Involuntary Movement Scale (AIMS) exam have been submitted AND the patient is ≥18 years of age. For re-approval, there must be documented clinical improvement.

*Public Comments:* Paul Isikwe from Teva Pharmaceuticals: Time yielded back to the committee.

Mark Golick from Neurocrine Biosciences: Time yielded back to the committee.

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

- **Select Contraceptive Agents**
  - No new drugs.
  - No other significant clinical changes.

**Recommendation:**

- Progestin Only Contraceptives:
  - Remove Ortho® Micronor (norethindrone) from the PDL.

- Vaginal Ring:
  - Add Nuvaring® (etonogestrel/ethinyl estradiol vaginal ring) to preferred. Move Etonogestrel/ethinyl estradiol vaginal ring to non-preferred.

- Topical Contraceptives:
  - Move Twirla® (levonorgestrel/ethinyl estradiol) patch to preferred. Add Zafemy (norelgestromin/ ethinyl estradiol) patch to preferred.

- Emergency Contraceptives:
  - Remove Take Action (levonorgestrel) from the PDL.

*Public Comments:* No public comment.

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

**12. Review of Newly-Developed/Revised Criteria:**

- Tranexamic Acid ®

Recommendation:

- Move Tranexamic acid (compare to Lysteda®) to preferred.
  - Clinical criteria:
    - Revise Lysteda: the patient has had a documented intolerance to the generic product.

*Public Comments:* none at this time.

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

**13. General Announcements:**

- None at this time.

**14. Adjourn:** Meeting adjourned at 7:55 p.m.