Department of Vermont Health Access
Pharmacy Benefit Management Program
DUR Board Meeting Minutes
September 14, 2021

Board Members Present:

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

Absent: N/A

Staff:

Laurie Brady, RPh, Change HealthCare
Carrie Germaine, DVHA
Nancy Hogue, Pharm D, DVHA
Lisa Hurteau, PharmD, DVHA
Jason Pope, DVHA
Jacqueline Hedlund, MD, Change Healthcare
Scott Strenio, MD, DVHA

Guests:

Adam Denman (Global Blood Therapeutics)
Archie Stone, PhD (Aurinia Pharmaceuticals)
Beth D'Ambrosio PharmD (Novartis)
Bethany Zanrucham PharmD (Sarepta Therapeutics)
Brian Dillon (Otsuka)
Frank Lanotte
Hannah Parker
Jai Persico (Nogen)
Joeseph Goble, PharmD, MS (Janssen)
Kristen Chopas
Laurian Sequeira
Lee Stout
Linda Burns
Lisa Dunn (Amgen)
Lisa Libera
Margaret Glassman
Mark Clark, MS (Zogeniz)
Melinda Given MS, PhD (United Therapeutics Corporation)
Megan Mays DNP, WHNP-BC (Eyofem Biosciences, Inc)
Nicholas Boyer (Braeburn)
Nicholas Primpas
Paul Iswke, PharmD
Peter Barrio (Teva Pharmaceuticals)
Rasheed Jandali
Rodney Francisco
Ronald Depue
Ryan Miller
Steven Burch, PhD, RPh
Taryn Stinson
Tina McCann
Tyson Thompson PharmD, MBA (Pfizer)
Zachary Spurlin, Pharm.D.

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 June meeting minutes were accepted as printed.

3. DVHA Pharmacy Administration Update: Nancy Hogue, Pharm.D., DVHA:

- DVHA is recruiting new board members. They are seeking 2 physicians and one member-at-large. Zail Berry and Patricia King's terms expired 8/31/21.
- The October DUR Board meeting encompasses the changes to support the 2022 Calendar Year supplemental rebate contracts. Executive session will begin at 5pm, and the public meeting will start at 6pm. The meeting will adjourn no later than 9pm.

4. Medical Director Update: Scott Strenio, MD, DVHA

- No updates at this time

6. Follow-up Items from Previous Meetings:

- None at this time

7. RetroDUR/ProDUR: Laurie Brady, RPH and Jacqueline Hedlund, MD, Change Healthcare

- Data Presentation: Influenza Vaccination Rates

Immunization guidelines published by the CDC recommend that everyone above the age of 6 months receive influenza vaccinations yearly unless there is a history of severe reactions to previous flu shots. Even those with egg allergies are eligible to get the vaccines, contrary to popular belief. Influenza is responsible for many thousands of deaths annually, including among children and those with chronic illnesses. It is somewhat surprising that more people are not immunized, given the many avenues available for immunization, including pharmacies, work sites, sponsored clinics, and PCP/medical specialty offices. While children are often the highest group affected by flu every year, immunization rates are lower than recommended. The federal government has the goal of vaccinating 70% of the population every year, however the data shows that less than half of Americans get the flu vaccine every year.

Change Healthcare used paid, non-reversed Medicaid pharmacy and medical claims from SFY 2019-2020 (pre-COVID), excluding members with Part D, VMAP and Healthy Vermonters coverage. They examined all of the medical and pharmacy claims for influenza vaccines for members who were eligible for vaccination in 2019 and determined the rate of vaccination for the 2019-20 flu season. This included looking at NDCs, CPT codes and administration codes for flu vaccines. Additionally, they looked at those who were prescribed oseltamivir, zanamivir and baloxavir in the 2018-2019 flu season to see if previous infection had any effect on improving vaccination rates compared to the general Medicaid population. Two high risk groups, children with asthma and adults with COPD, were examined to see if there was a better vaccination rate than that of the general Medicaid population given the higher likelihood of severe infection and death. One possible limitation is that not all claims may have been submitted to Medicaid due to the Vermont Children's Vaccination Program (VCVP) providing free vaccines and providers only are reimbursed for administration.

The percentage of members vaccinated in the high-risk groups was higher than that of the general Medicaid patient population. Forty-four percent (44%) of Adults with COPD received a vaccine compared with 23% of all adults. Forty-five percent (45%) of children with asthma received a vaccine compared with 33% of all children. The total number of members who

received treatment for influenza in SFY 2019 was 1,148. Of those members, 477 (42%) received the influenza vaccine the following year (SFY 2020). This represents a higher percentage than the general Medicaid population, of which only 28% received the vaccine.

Recommendation: Vaccination rates according to this review are lower than the current vaccination goals. This may be due to members' willingness or attention to getting the vaccine. Influenza vaccines are now widely available in the community and access is widespread. Educating providers about the low vaccination rates in Vermont is advisable as a reminder of the unmet need in the broader community and those at highest risk. We also recommend that DVHA share this data with the Department of Health's Asthma Advisory Committee and Tobacco Cessation Programs to explore opportunities for collaboration.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- Data Presentation: Long-Acting Injectable Antipsychotics

One of the challenges of treating people with schizophrenia is compliance with daily oral medication regimens. It is estimated that the adherence rate is less than 60%. The side effect profile with antipsychotics, both short and long term contributes to low adherence. Additionally, patients may still hallucinate or have delusions that convince them to stop taking medications, even when they were being taken appropriately. In patients who struggle with medication adherence, there is the option of every 2 week or once monthly injectable long-acting antipsychotics (LAIs), either given IM or SC. This strategy can be employed in those who have a history of adequate response to oral treatment, but relapse due to non-adherence. Using long-acting antipsychotics can prevent hospitalizations and are a way to deal with issues that complicate compliance, such as substance use, lack of stable housing or social structure, and unstable disease. Using LAIs can identify patients who have refractory disease due to compliance alone, versus those who have a sub-optimal response to oral treatment. Additionally, some patients may have a better response to a consistent blood level of drug, rather than the peaks and troughs that come with oral formulations. Some may find side-effects less bothersome. However, there are still potential issues with compliance since patients need to stay on a schedule and appear at the provider's office to receive the injections. Concern is that there may be excessive waste in the system if patients miss appointments or refuse the injection. Often LAIs are provided through "white bagging" which means prescriptions are filled, typically by a mail order or specialty pharmacy, and shipped to the provider office or clinic. Because they are labeled for an individual patient, they are not reusable for another patient. Additionally, injectable antipsychotic medications are substantially more costly than oral formulations.
Change Healthcare used paid, non-reversed Medicaid pharmacy and medical claims from calendar year 2019 (pre-COVID), excluding members with Part D or other insurance as primary coverage, VMAP, and Healthy Vermonters coverage. They looked at all pharmacy claims for monthly LAIs in calendar year 2019 and then attempted to determine if the monthly

prescriptions filled at the pharmacy level were administered by looking to see if an appropriate CPT code was billed within 14 days of pharmacy billing.

The following CPT codes were used in the analysis:
96372: Therapeutic, prophylactic, or diagnostic injection
90792: Psychiatric Diagnostic Procedures
99211, 99212, 99213, 99214, 99215: Established Patient Office or Other Outpatient Services
99417: Prolonged Service on the Date of an Office or Other Outpatient Service

5 antipsychotics that can be administered on every 4-week schedules were included in the analysis: Invega Sustenna®, Aristada® (except 882mg), Abilify Maintena®, Perseris®, and Haloperidol Decanoate. The goal of the analysis was to evaluate compliance, persistence, and waste.

A majority of the doses of LAIs have no corresponding injection code. Therefore, the ability of this DUR to assess waste was very limited. In speaking with a few providers who ordered the drug, they were unaware of a separate injection code or are not billing for it. Of note, these offices were able to confirm that the medication was administered, and this was included within the patient's record.

Recommendation: Due to the limitations of the analysis, DVHA was unable to determine if doses were wasted, and if so, how many. DVHA Pharmacy Unit will share these findings with the Reimbursement Unit to ascertain whether any outreach to providers is warranted.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- ProDUR is an integral part of the Vermont Medicaid claims adjudication process.

ProDUR includes:

- Reviewing claims for therapeutic appropriateness before the medication is dispensed;
- Reviewing the available medical history;
- Focusing on those patients at the highest severity of risk for harmful outcome; and
- Intervening and/or counseling when appropriate.

Prospective Drug Utilization Review (ProDUR) encompasses the detection, evaluation, and counseling components of pre-dispensing drug therapy screening. The ProDUR system addresses situations in which potential drug problems may exist. ProDUR performed prior to dispensing assists pharmacists in ensuring that patients receive appropriate medications. This is accomplished by providing information to the dispensing pharmacist that may not have been previously available.

Because ProDUR examines claims from all participating pharmacies, drugs which interact or are affected by previously dispensed medications can be detected. While the pharmacist uses his/her education and professional judgment in all aspects of dispensing, ProDUR is intended an informational tool to aid the pharmacist.

The following ProDUR Reason of Service types will deny for the Vermont Medicaid program:

- Drug-to-Drug Interaction (Highest Severity Levels Only)
- Therapeutic Duplication

ProDUR Edits that deny may be overridden at POS using the interactive NCPDP DUR override codes. When a claim is rejected for a DUR edit, pharmacies may override the denial by submitting the appropriate Professional Service and Result of Service codes.
The valid DUR Reason for Service Codes for Vermont Medicaid are:

DD - Drug-Drug Interaction
TD - Therapeutic Duplication

The only acceptable Professional Service Codes are:

MR – Medication Review
M0 – Prescriber Consulted
R0 – Pharmacist Consulted Other

Nancy Hogue, PharmD, DVHA, advised the board that CMS considers ProDUR part of the dispensing activities, therefore, these professional services are included in the dispensing fee.

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

Biosimilar Drug Reviews:

- None at this time.

Full New Drug Reviews:

- Amondys® 45 (casimersen)

Casimersen, the active ingredient of Amondys® 45, is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass. PMOs are synthetic molecules in which the 5-membered ribofuranosyl rings found in natural DNA and RNA are replaced by a 6-member morpholino ring. Casimersen is designed to bind to exon 45 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 45 skipping. Exon 45 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 45 skipping. It is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping. This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Amondys® 45. Continued approval for this indication may be contingent upon verification of a clinical benefit

in confirmatory trials. The safety and efficacy of Amondys® 45 on dystrophin production was assessed in one study that included male DMD patients who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping. This study 1 is an ongoing, double-blind, placebo-controlled, multicenter study designed to assess the safety and efficacy of Amondys® 45 in ambulatory patients. This study is planned to enroll a total of 111 patients, aged 7 to 13 years, randomized to Amondys® 45 or placebo. Patients were required to have been on a stable dose of oral corticosteroids for at least 24 weeks prior to dosing with Amondys® 45 or placebo. Following the 96 week double-blind period, all patients began or were to begin an additional 48 week open-label treatment period. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials. Interim analysis of an ongoing double-blind, placebo-controlled trial demonstrated statistically significantly greater mean dystrophin levels at week 48 from baseline with Amondys® 45 compared with placebo.

Recommendation:

- Add Amondys 45 (casimersen) to non-preferred.
- Note that all products require a PA in this class.
    - Clinical criteria:
        - Add Amondys to the Exondys, Viltepso, Vyondys criteria:
          • The patient must have a diagnosis of Duchenne Muscular Dystrophy with a confirmed mutation of the DMD gene that is amenable to exon 45 skipping (for Amondys) or exon 51 skipping (for Exondys) or exon 53 skipping (for Viltepso, Vyondys) (results of genetic testing must be submitted) AND
          • The prescriber is, or has consulted with, a neuromuscular disorder specialist AND
          • The dose does not exceed 30mg/kg once weekly (for Amondys, Exondys, Vyondys) or 80mg/kg once weekly (for Viltepso) AND
          • The patient is currently on a stable corticosteroid dose for at least 6 months.
          • Note: Initial approval will be granted for 6 months. For re-approval after 6 months, the patient must demonstrate a response to therapy as evidenced by continued or improved clinically meaningful function.

Public Comment: Bethany Zanrucha from Sarepta Therapeutics: Highlighted the attributes of Amondys 45.

Board Decision: The Board unanimously approved the above recommendations.

- Bronchitol® (mannitol)

D-Mannitol (referred to throughout as mannitol), the active ingredient of Bronchitol®, is a hexahydric sugar alcohol. The exact mechanism of action for its approved indication is not known. It is indicated as an add-on maintenance therapy to improve pulmonary function in

adult patients 18 years and older with cystic fibrosis (CF). Use Bronchitol® only for adults who have passed the Bronchitol® Tolerance Test (BTT). The safety and efficacy of Bronchitol® for the treatment of CF were assessed in 3 randomized, double-blind, controlled studies that were 26 weeks in duration. Study 1 included adults ≥18 years of age with baseline FEV1 >40 to <90% of predicted. Adults treated with Bronchitol® resulted in a statistically significant improvement in FEV1; the treatment difference between Bronchitol® and control for the adjusted mean change in FEV1 from baseline over 26 weeks was 51ml. There is no evidence at this time to support that Bronchitol® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation:

- Add Bronchitol® (mannitol) capsules for inhalation with QTY LIMIT: 560 capsules/28 days; maximum day supply = 28 days to non-preferred.
  - Clinical criteria:
    - Add Bronchitol: Diagnosis or indication is cystic fibrosis AND the patient is 18 years of age or older AND the patient has a documented inadequate response or contraindication to hypertonic saline and Pulmozyme AND the patient has passed the Bronchitol Tolerance Test (BTT) AND the patient has been counseled to use a short-acting beta agonist (SABA) 5-15 minutes prior to each dose.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- Evkeeza® (evinacumab-dgnb)

Evinacumab-dgnb, the active ingredient of Evkeeza®, is an angiopoietin-like protein 3 (ANGPTL3) inhibitor monoclonal antibody (IgG4 isotype) produced by recombinant DNA technology in Chinese hamster ovary (CHO) cell suspension culture. It binds to and inhibits ANGPTL3. ANGPTL3 is a member of the angiopoietin-like protein family that is expressed mainly in the liver and plays a role in the regulation of lipid metabolism by inhibiting lipoprotein lipase (LPL) and endothelial lipase (EL). Evinacumab-dgnb inhibition of ANGPTL3 leads to reduction in LDL-C, HDL-C, and triglycerides (TG). Evinacumab-dgnb reduces LDL-C independent of the presence of LDL receptor (LDLR) by promoting very low-density lipoprotein (VLDL) processing and clearance upstream of LDL formation. Evinacumab-dgnb blockade of ANGPTL3 lowers TG and HDL-C by rescuing LPL and EL activities, respectively. It is indicated as an adjunct to other low-density lipoprotein cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH). The safety and efficacy of Evkeeza® have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH). The safety and efficacy of Evkeeza® were assessed in a multicenter, randomized, double-blind, placebo-controlled trial (ELIPSE-HoFH) that compared Evkeeza® with placebo in patients with HoFH for 24 weeks. The effects of Evkeeza® on

cardiovascular morbidity and mortality have not been determined and clinical trial experience has been limited as evidenced by the small sample size in the registration study, ELIPSE-HoFH. In this small placebo-controlled study, the least squares mean treatment difference between Evkeeza® and placebo in mean percent change in LDL-C from baseline (the primary endpoint) was -49%, which was statistically significant (p<0.0001). Comparator trials with other agents were not found.

Recommendation:

- Add Evkeeza™ (evinacumab-dgnb) intravenous solution to non-preferred.
  - Clinical criteria:
    - Revise Juxtapid and Add Evkeeza:
      Total cholesterol > 290mg/dL or LDL-C > 190mg/dL (adults) OR Total cholesterol levels > 260mg/dL or LDL-C > 155mg/dL (children < 16 years) and TG within reference range or Confirmation of diagnosis by gene testing AND Documented adherence to prescribed lipid lowering medications for the previous 90 days AND Recommended or prescribed by a lipidologist or Cardiologist AND Inability to reach goal LDL-C despite a trial of 2 or more maximum tolerated dose of statins (one of which must be atorvastatin or rosuvastatin), ezetimibe 10mg daily, and Repatha

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- Gemtesa® (vibegron)

Vibegron, the active ingredient of Gemtesa®, is a selective beta-3 adrenergic receptor agonist. Activation of the beta-3 adrenergic receptor increases bladder capacity by relaxing the detrusor smooth muscle during bladder filling. It is indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults. The safety and efficacy of Gemtesa® were assessed in a 12-week double-blind, randomized, placebo-controlled and active-controlled study that included patients with OAB. In a 2021 meta-analysis by Su et al4, the authors concluded that the therapeutic effect of vibegron was similar to that of antimuscarinic therapy, but that vibegron did not increase the risk of adverse events (e.g. dry mouth). Serious adverse events and discontinuations due to adverse events were not significantly different between treatment groups. In addition, while no formal comparators have been made, Gemtesa® does not have a warning regarding increased blood pressure as does Myrbetriq® (mirabegron), a previously FDA approved beta-3 adrenergic receptor agonist. Although blood pressure increases, like those seen with Myrbetriq® (another FDA approved beta-3 adrenergic receptor agonist) were not observed during Gemtesa® trials, it is important to note that head-to-head studies between the two agents have not been performed. Therefore, it is concluded that while there is some preliminary data that vibegron may be better tolerated with regards to some side effects, the efficacy appears to be similar to antimuscarinics and the tolerability comparison should be demonstrated in head-to-head trials. It is therefore recommended that Gemtesa® remain non-preferred and require prior

authorization and be available to those who are unable to tolerate or who have failed on more cost-effective, preferred medications.

- Vesicare® LS (solifenacin)

Solifenacin, the active ingredient of Vesicare® LS, is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergic mediated functions, including contractions of urinary bladder smooth muscle. The safety and efficacy of Vesicare® LS oral suspension were assessed in two 52-week, open-label, baseline-controlled, sequential dose titration studies that included pediatric patients 2 year of age and older (N=95) with neurogenic detrusor overactivity (NDO). Study 1 included patients 2 to less than 5 years of age (N=19) and study 2 included patients 5 to 17 years of age (N=76). Entry criteria required that patients had a diagnosis of NDO confirmed by urodynamics demonstrating the presence of involuntary detrusor contractions with detrusor pressure increase greater than 15cm H2O and that patients or their caregivers practiced clean intermittent catheterization (CIC). Of the patients in study 1, 17 completed treatment through week 24 and had adequate urodynamic measurements for evaluation of efficacy. Of the patients in study 2, 49 patients (24 patients aged 5 to <12 and 25 patients aged 12 to 17 years) completed treatment through week 24 and had adequate urodynamic measurements for evaluation of efficacy. The primary efficacy endpoint was change from baseline in the patient's maximum cystometric (bladder) capacity (MCC) after 24 weeks of treatment with Vesicare® LS. An improvement in MCC was observed in patients aged 2 to less than 5 years of age and in patients aged 5 to 17 years of age. The magnitude of the changes from baseline in the primary and secondary efficacy endpoints were comparable between patients 5 to less than 12 years of age and patients 12 to 17 years of age. There is no evidence at this time to support that Vesicare® LS is safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Vesicare® LS be non-preferred

Recommendation:

- Add Gemtesa® (vibegron) tablet with QTY LIMIT: 1 tablet/day to non-preferred. Add Vesicare® LS (solifenacin) oral suspension to non-preferred.
- Move MYRBETRIQ® (mirabegron) ER Tablet with QTY LIMIT: 1 tablet/day to preferred.
    - Clinical criteria:
        - Add Gemtesa: The patient has had a documented side effect, allergy, treatment failure, or contraindication with one preferred long-acting urinary antimuscarinic agent and Myrbetriq.
        - Add Vesicare LS: The patient has a diagnosis of neurogenic detrusor activity AND the patient has a documented side effect, allergy, or treatment failure with oxybutynin AND for patients ≥ 18 years of age, medical necessity has been provided for a liquid formulation.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- Lupkynis® (voclosporin)

Voclosporin, the active ingredient of Lupkynis®, is a calcineurin-inhibitor immunosuppressant. The mechanism of action has not been fully established. Activation of lymphocytes involves an increase in intracellular calcium concentrations that bind to the calcineurin regulatory site and activate calmodulin binding catalytic subunit and through dephosphorylation activates the transcription factor, Nuclear Factor of Activated T-Cell Cytoplasmic (NFATc). The immunosuppressant activity results in inhibition of lymphocyte proliferation, T-cell cytokine production, and expression of T-cell activation surface antigens. It is indicated in combination with a background immunosuppressive therapy regimen for the treatment of adult patients with active lupus nephritis (LN). The safety and efficacy of Lupkynis® have not been established in combination with cyclophosphamide. Use of Lupkynis® is not recommended in this situation. The safety and efficacy of Lupkynis® were assessed in a 52-week, randomized, double-blind, placebo-controlled study that included adults diagnosed with systemic lupus erythematosus and with International Society of Nephrology/Renal Pathology Society (ISN/RPS) biopsy-proven active Class III or IV lupus nephritis (LN) (alone or in combination with Class V LN) or Class V LN. Patients with Class III or IV LN (alone or in combination with Class V LN) were required to have a urine protein to creatinine (UPCR) ratio of ≥1.5mg/mg; patients with Class V LN were required to have a UPCR of ≥2mg/mg. A baseline eGFR must be established before the start of treatment and use is not recommended in patients with a baseline eGFR ≤45ml/min/1.73m2. In addition, blood pressure must be checked at baseline and treatment should not be started in patients with BP >165/105mmHg or with hypertensive emergency. In the randomized, double-blind clinical trial assessing the safety and efficacy of Lupkynis®, a significantly higher proportion of patients in the Lupkynis®/MMF/corticosteroid arm than the placebo/MMF/corticosteroid arm achieved complete renal response at week 52. Other comparator studies were not found.

Recommendation:

- Add Lupkynis™ capsule to non-preferred
  - Clinical Criteria:
    - Add Lupkynis: The patient has a diagnosis of Systemic Lupus Erythematosus (SLE) AND The patient has active Lupus Nephritis confirmed by urine/blood tests or kidney biopsy AND The patient is ≥ 18 years of age AND Medication is prescribed by, or in consultation with, a nephrologist or rheumatologist AND The patient has clinical progression (e.g. worsening of proteinuria or serum creatinine) after 3 months of induction therapy with corticosteroids plus cyclophosphamide or mycophenolate mofetil OR failure to respond after 6 months of induction therapy with corticosteroids plus cyclophosphamide or mycophenolate

mofetil AND Medication will be used in combination with background immunosuppressive therapy (e.g. mycophenolate mofetil and systemic corticosteroids) AND The patient has a documented intolerance or treatment failure with Benlysta

Public Comment: Archie Stone, PhD from Aurinia Pharmaceuticals: Highlighted the attributes of Lupkynis.

Board Decision: The Board unanimously approved the above recommendations.

- Ponvory® (ponesimod)

Ponesimod, the active ingredient of Ponvory®, is a sphingosine 1-phosphate (S1P) receptor 1 modulator that binds with high affinity to S1P receptor 1. Ponesimod blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which ponesimod exerts therapeutic effects in multiple sclerosis is not known but may involve reduction of lymphocyte migration into the CNS. It is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. The safety and efficacy of Ponvory® were assessed in a randomized, double-blind, parallel group, active-controlled superiority study that included patients with relapsing forms of MS who were treated for 108 weeks. Due to a decrease in heart rate with Ponvory® initiation, a first-dose 4-hour monitoring is recommended for patients with sinus bradycardia, first-or second-degree AV block, or a history of MI or heart failure occurring more than 6 months prior to treatment initiation and in stable condition. Advice from a cardiologist should be sought to determine the most appropriate monitoring strategy during treatment initiation if treatment is started in certain patients (e.g. with prolonged QTc interval or with some pre-existing heart and cerebrovascular conditions). A phase 3 double-blind, superiority study compared Ponvory® with teriflunomide 14mg and results suggested that the ARR was statistically significantly lower in those treated with Ponvory® as compared with teriflunomide 14mg. While no statistically significant differences were observed in confirmed disability progression, the number of Gd-enhancing T1 lesions and the number of new or enlarging T2 lesions were statistically significantly lower in the Ponvory® group than in the teriflunomide group.

Recommendation:

- Add Ponvory™ (ponesimod) tablet with QTY LIMIT: 1 tablet/day; Maximum 30-day supply per fill to non-preferred.
  - Clinical criteria:
    - Revise Mayzent, Ponvory, Zeposia: Diagnosis of relapsing-remitting MS, Clinical Isolated Syndrome or Active Secondary Progressive MS (SPMS): Patient is ≥ 18 years AND Patient CYP2C9 variant status has been tested to determine genotyping (Mayzent only; required for dosing; therapy is contraindicated in CYP2C9*3/*3) AND Baseline CBC, electrocardiogram (ECG), and ophthalmic evaluation have

been completed AND Patient has a documented side effect, allergy, treatment failure or contraindication to at least two preferred drugs, one of which must be Gilenya.

Public Comment: Joe Goble, PharmD from Janssen Pharmaceuticals: Highlighted the attributes of Ponvory.

Board Decision: The Board unanimously approved the above recommendations.

- Qdolo® (tramadol HCL solution)

Tramadol, the active ingredient of Qdolo®, is an opioid agonist and inhibitor of norepinephrine and serotonin re-uptake. Although the mechanism of action is not completely understood, the analgesic effect of tramadol is believed to be due to both binding to μ-opioid receptors and weak inhibition of re-uptake of norepinephrine and serotonin. Analgesia in humans begins approximately within one hour after administration and reaches a peak in about 2 to 3 hours. It is indicated in adults for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of the risk of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Qdolo® for use in patients for whom alternative treatment options (e.g. non-opioid analgesics): Have not been tolerated or are not expected to be tolerated, Have not provided adequate analgesia or are not expected to provide adequate analgesia.
Tramadol has been given in single oral doses of 50mg, 75mg, and 100mg to patients with pain following surgical procedures and pain following oral surgery. It has been studied in 3 long-term trials involving patients with a variety of chronic painful conditions. Tramadol tablets, under the brand name Ultram®, have been available for many years, have been found to be safe and effective, and have the same indication as Qdolo®. The studies included in the Qdolo® prescribing information were the same as found in the Ultram® prescribing information. Ultram® tablets are available as a generic. The efficacy of Qdolo® was based on that of immediate-release tramadol tablets, which have been available for numerous years and been found to be safe and effective.

Recommendation:

- Add Qdolo® (tramadol) oral solution to non-preferred.
  - Clinical criteria:
    - Add Qdolo: The patient is ≥ 18 years of age AND medical necessity has been provided for a liquid formulation AND the patient has had a documented side effect, allergy or treatment failure with oxycodone oral solution and morphine oral solution.

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

- Verquvo® (vericiguat)

Vericiguat, the active ingredient of Verquvo®, is a soluble guanylate cyclase stimulator. Soluble guanylate cyclase (sGC) is an important enzyme in the nitric oxide (NO) signaling pathway. When NO binds to sGC, the enzyme catalyzes the synthesis of intracellular cyclic guanosine monophosphate (cGMP), a second messenger that plays a role in the regulation of vascular tone, cardiac contractility, and cardiac remodeling. Heart failure is associated with impaired synthesis of NO and decreased activity of sGC, which may contribute to myocardial and vascular dysfunction. By directly stimulating sGC, independently of and synergistically with NO, vericiguat augments levels of intracellular cGMP, leading to smooth muscle relaxation and vasodilation. It is indicated to reduce the risk of cardiovascular death and heart failure (HF) hospitalization following a hospitalization for heart failure or need for outpatient IV diuretics, in adults with symptomatic chronic HF and ejection fraction less than 45%. The efficacy of Verquvo® was assessed in a randomized, double-blind, placebo-controlled, parallel-group, event-driven, multicenter study (VICTORIA) that included adult patients with symptomatic chronic heart failure (New York Heart Association [NYHA] class II-IV) and left ventricular ejection fraction (LVEF) less than 45% following a worsening heart failure event. A worsening heart failure event was defined as heart failure hospitalization within 6 months before randomization or use of outpatient IV diuretics for heart failure within 3 months before randomization. In this analysis, SGLT2i were found to be more effective than sacubitril/valsartan and vericiguat, although statistical significance was not reached for the most clinically relevant outcomes of CV death or HF hospitalization and CV death alone. The authors concluded that based on indirect comparisons, SGLT2 inhibitor therapy is not associated with a significantly lower risk of cardiovascular death or HF hospitalization or cardiovascular death alone compared to sacubitril/valsartan or vericiguat. The risk of HF hospitalization did not differ significantly between patients on SGLT2 inhibitors or sacubitril/valsartan, while dapagliflozin was superior to vericiguat.

Recommendation:

- Add new sub-category Soluble Guanylate Cyclase (sGC) Stimulators and note that all products require PA.
- Add Verquvo® (vericiguat) tablet with QTY LIMIT: 1 tablet/day to non-preferred.
  - Clinical criteria:
    - Add Verquvo: The diagnosis or indication is symptomatic heart failure (HF) with ejection fraction < 45% AND the patient has been hospitalized for HF within the previous 6 months or required the use of IV diuretics within the past 3 months AND the patient is not pregnant AND the patient is concurrently receiving the maximum tolerated dose of one agent from each of the following classes, unless contraindicated:
      - ARNI, ACE-I, or ARB
      - Beta Blocker (metoprolol, carvedilol, or bisoprolol)
      - Aldosterone antagonist if LVEF ≤ 35% or LVEF ≤ 40% with diabetes mellitus or post myocardial infarction (MI) with HF symptoms

Public Comment: None at this time.

Board Decision: The Board unanimously approved the above recommendations.

9. New Therapeutic Drug Classes

- None at this time.

10. Therapeutic Drug Classes- Periodic Review:

- **Androgenic Agents**
  - No new drugs.
  - No new significant clinical changes.

Recommendation:

- Remove Axiron (testosterone 2% solution) from the PDL.
- Add Natesto® (testosterone) nasal gel with QTY LIMIT: 3 bottles/30 days to non-preferred.
  - Clinical criteria:
    - Add Natesto: The patient has had a documented side effect, allergy, or treatment failure to TWO preferred testosterone products (topical and/or injectable formulations).

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- **Antiemetics**
  - No new drugs.
  - No new significant clinical changes.

Recommendation:

- Remove Anzemet® (dolansetron) 100 mg, Emend (aprepitant) 40mg and 125mg tablets, and Zofran® (ondansetron) injection, oral solution 4 mg/5 ml, 8mg tablets, and orally disintegrating tablets from the PDL.
- Move ONDANSETRON oral solution 4mg/5mL to preferred.
- Move Diclegis (10 mg doxylamine succinate and 10 mg pyridoxine hydrochloride) DR tablet with QTY LIMIt: 4 tablets/day to preferred.
  - Clinical criteria:
    - Revise Zofran: patient must have a documented intolerance to the generic formulation.
    - Revise Bonjesta, Doxylamine/Pyridoxine: patient has a documented intolerance to Diclegis.

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- **Antipsychotics**
  - No new drugs.
  - The original Seroquel® (AstraZeneca) trials studied, as secondary outcomes, insomnia ratings. And, across trials, Seroquel was an effective sedative/hypnotic AND anxiolytic. The FDA did not approve for insomnia or generalized anxiety disorder (GAD), however, as they believed the risk of weight gain, diabetes, and dyslipidemia was too high. However, in many folks at low doses these problems can often be managed with appropriate monitoring. Low dose quetiapine can a good strategy for some patients with chronic anxiety. There is clinical trial data to support the use of low dose quetiapine, and with many available generics is now a cost-effective therapy

Recommendation:

- Add Asenapine sublingual tablet (compare to Saphris®) with FDA maximum recommended dose = 20 mg/day, Aripiprazole oral solution with FDA maximum recommended dose = 25 mg/day, and Aripiprazole ODT with QTY Limit: 10mg and 15mg=2 tabs/day and FDA maximum recommended dose = 30 mg/day to non-preferred.
- Move all strengths of Quetiapine to preferred.
- Remove Abilify® (aripiprazole) oral solution, Abilify® (aripiprazole) Discmelt, and Risperdal® M (risperidone) from the PDL.
  - Clinical criteria:
    - Remove Note: Trazodone dosed at < 150mg/day will not be considered as a trial for adjunct treatment of MDD or any anxiety disorder. Bupropion will not be considered as a trial for adjunct treatment of any anxiety disorder.
    - Add Asenapine to the Invega, Paliperidone, Saphris clinical criteria: The indication for use is the treatment of schizophrenia/schizoaffective disorder or bipolar disorder AND The patient has had a documented side effect, allergy, or treatment failure with at least three two preferred products (typical or atypical antipsychotics), one of which is risperidone.
    - Add aripiprazole oral solution: the patient has had a documented side effect, allergy or treatment failure with preferred risperidone oral solution.

Public Comments: Steven Burch, PhD, RPh from Sunovion Pharmaceuticals: Time yielded back to the committee.

Board Decision: The Board unanimously approved the above recommendations.

- **Pulmonary Agents: Beta-Agonists, COPD Agents, and Inhaled Corticosteroids**
  - No new drugs.
  - Updates to GOLD Guidelines have been discussed at previous DUR Board meetings.

Recommendation:

Pulmonary Agents

Anticholinergics: Inhaled

- Move Incruse Ellipta® (umeclidinium bromide) with QTY LIMIT: 3 inhalers/90 days and Stiolto® Respimat (tiotropium/olodaterol) with QTY LIMIT: 3 inhalers/90 days to preferred. Move Bevespi Aerosphere® (glycopyrrolate/formoterol) with QTY LIMIT: 3 inhalers/90 days to non-preferred.
- Revise clinical criteria for Tudorza: The patient has had a documented side effect, allergy, or treatment failure with a preferred LAMA.

Beta-Adrenergic Agents

- Add Arformoterol (compare to Brovana®) with QTY LIMIT: 2 vials/day and Formoterol (compare to Perforomist®) with QTY LIMIT: 2 vials/day to non-preferred. Remove Metaproterenol tablets/syrup from the PDL.

Corticosteroids/Combinations: Inhaled

- Revise clinical criteria for Budesonide Inh Suspension: Medical necessity for the use of a nebulized solution has been provided AND if the dose is 1mg, the patient must be unable to use two 0.5 mg vials.
- Revise clinical criteria for Pulmicort Respules: Medical necessity for the use of a nebulized solution has been provided AND if the dose is 1 mg, the patient must be unable to use two 0.5 mg vials AND the patient has a documented intolerance to the generic.

Phosphodiesterase-4 (PDE-4) Inhibitors

- Add note that all products require a PA.

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

- **Growth Hormones**
  - No new drugs.
  - No other significant clinical changes.

Recommendation:

- None at this time.

Public Comments: No public comment.

Board Decision: None needed at this time.

- **Pulmonary Arterial Hypertension Medications**
  - No new drugs.
  - Tyvaso® (Treprostinil) is now approved for the treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability.

Recommendation:

- None at this time.

Public Comments: Melinda Given, MS, PHD from United Therapeutics Corporation highlighted the attributes of Tyvaso®.

Board Decision: None needed at this time.

12. Review of Newly-Developed/Revised Criteria:

- **Benlysta® (belimumab)**
  - In late December 2020, The FDA approved belimumab to treat adults with active lupus nephritis who are receiving standard therapy. This approval if for both the intravenous and subcutaneous formulations.

Recommendation:

Clinical criteria:

Indication for use is Systemic Lupus Erythematosus (SLE):

- The patient is positive for autoantibodies (anti-nuclear antibody (ANA) and/or anti-double-stranded DNA (anti-dsDNA) AND
- The patient has had a documented inadequate response or intolerance to at least TWO of the following agents: NSAIDs, hydroxychloroquine, corticosteroids, azathioprine, methotrexate, mycophenolate mofetil AND
- Initial approval will be granted for 3 months. For therapy continuation, clinical documentation must be submitted documenting stable disease activity OR reduction in disease activity or corticosteroid dose. Note: The efficacy of Benlysta® has not been evaluated in patients with severe active central nervous system lupus. Benlysta has not been studied in combination with other biologics

or intravenous cyclophosphamide. Use of Benlysta is not recommended in these situations.

Indication for use is Active Lupus Nephritis:

- Diagnosis has been confirmed by urine/blood tests or kidney biopsy AND
- The patient is ≥ 18 years of age AND
- Medication is prescribed by, or in consultation with, a nephrologist or rheumatologist AND
- The patient has clinical progression (e.g. worsening of proteinuria or serum creatinine) after 3 months of induction therapy with corticosteroids plus cyclophosphamide or mycophenolate mofetil OR failure to respond after 6 months of induction therapy with corticosteroids plus cyclophosphamide or mycophenolate mofetil AND
- Medication will be used in combination with background immunosuppressive therapy (e.g. mycophenolate mofetil and systemic corticosteroids) AND
- Initial approval will be granted for 3 months. For therapy continuation, clinical documentation must be submitted documenting stable disease activity OR reduction in disease activity. Note: The efficacy of Benlysta® has not been evaluated in patients with severe active central nervous system lupus. Benlysta has not been studied in combination with other biologics or intravenous cyclophosphamide. Use of Benlysta is not recommended in these situations. Initial approval will be granted for 3 months. For therapy continuation, clinical documentation must be submitted documenting stable disease activity OR reduction in disease activity or corticosteroid dose.

Public Comments: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

13. General Announcements:

- FDA Approves First Interchangeable Biosimilar Insulin Product for Treatment of Diabetes
  https://www.fda.gov/news-events/press-announcements/fda-approves-first-interchangeable-biosimilar-insulin-product-treatment-diabetes?utm_medium=email&utm_source=govdelivery

14. Board Discussion:

Margot Kagan asked if any follow information was available regarding the RetroDUR topic of Codeine Use in Pediatrics (presented at a previous meeting). The Board was looking for utilization information on pediatric use of other opioids such as morphine. This data is currently being worked on and forthcoming. Dr. Nasca also expressed concern about under treating pain in the pediatric population in light of the FDA warning of codeine use in children.

15. Adjourn: Meeting adjourned at 8:25 p.m.