Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

Maine Department of Health and Human Services
Office of MaineCare Services - Pharmacy Unit
11 State House Station
Augusta, Maine 04333-0011
Toll Free: (866) 796-2463; TTY: Dial 711 (Maine Relay)
Fax: (207) 287-8601

TO: Maine Drug Utilization Review Board
DATE: 06/16/22
RE: Maine DUR Board Meeting minutes from June 14, 2022

ATTENDANCE	PRESENT	ABSENT	EXCUSED
Linda Glass, MD			X
Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR			X
Kathleen Polonchek, MD	X		
Erin Ackley, PharmD.	X		
Corinn Normandin, PharmD.	X		
Caitlin Morrow, PharmD.	X		
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare	X		
Jacquelyn Hedlund, MD, Change Healthcare	X		
Anne-Marie Toderico, PharmD MaineCare Pharmacy Director	X		

Guests of the Board: Fran Jensen, OMS Medical Director

CALL TO ORDER: 6:30PM

Erin Ackley called the meeting to order at 6:30 PM.

PUBLIC COMMENTS

Hannah Longley from NAMI Maine: Highlighted to the DUR committee on behalf of our members that patient factors should also be taken into consideration when making formulary decisions.
Nitin Beri from Genetech: Highlighted the attributes of Vabysmo.
Victoria Romo-Le Tourneau from Pfizer: Highlighted the attributes of Cibinqo.
Christopher Ngai from Calliditas: Highlighted the attributes of Tarpeyo.
Chikezie Okoro from Bristol Myers Squibb: Highlighted the attributes of Opdualag.
Timothy Birner from Alkermes: Highlighted the attributes of Lybalvi.
Beth D'Ambrosio from Novartis: Highlighted the attributes of Vijoice.
Jannetta Bekman from Abbvie: Highlighted the attributes of Vraylar.

OLD BUSINESS

DUR MINUTES

Approval of March 08, 2022, DUR meeting minutes.

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE- ANNE-MARIE TODERICO

- Thanked Kenneth "Mac" McCall, PharmD, BCGP, FAPhA, and Corinn Normandin, PharmD, BCACP, CDOE for their distinguished service to the MaineCare Drug Utilization Review committee.
- Welcomed Caitlin Morrow, PharmD, BCACP, to the MaineCare Drug Utilization Review committee. She is joining this month as a non-voting member and will be a voting member at our September 2022 meeting.
- Shared that through our partnership with the Governor's Opioid Response Clinical Advisory Committee, MaineCare adapted our buprenorphine/naloxone prior authorization (PA) requirements and have increased access to medications for the treatment of opioid use disorder. A recent claim review showed a 46% reduction in the number of PAs.
- MaineCare implemented a Biosimilar Preferred Drug List (PDL) on the medical benefit. MaineCare will now designate preferred and non-preferred medications for infliximab, pegfilgrastim, bevacizumab and trastuzumab. The Biosimilar PDL rule making is final and the PDL aligns with our pharmacy PDL. The rule will be enforced beginning July 13. This gives providers two months to work through their current stock of non-preferred agents

REVISED CLINICAL CRITERIA/PREFERRED REVIEW

Spravato criteria:

Spravato: Treatment Resistant Depression

• Must be 18 years of age or older; and medication must be administered under the direct, on site, supervision of a licensed healthcare provider with post-administration observation of a minimum of least 2-hours. The medication must be prescribed by or in consultation with a psychiatrist and prescriber must be enrolled in the REMS program.

• Approval is based upon failure of at least two antidepressants and failure of an antidepressant used adjunctively with one recognized augmentation strategy such as lithium, an atypical antipsychotic, thyroid hormone, etc

• Ongoing use of Spravato beyond 3 months is based upon a positive response as evidenced by at least a 30 % reduction from baseline as measured by a standardized rating scale including PHQ 9, Hamilton Depression Rating Scale, or QIDS).

Spravato: MDD with Suicidal Ideation

Approval for this indication only if it is started in an inpatient unit, given adjunctively with an optimized antidepressant regimen, and with an 8-12 week initial approval with ongoing use dependent upon documentation of ongoing benefit.

Invega Hafyera criteria:

Invega Hafyera: The patient is started and stabilized on the medication OR The patient has been adequately treated with Invega Sustenna (paliperidone palmitate 1-month) for at least four months or Invega Trinza (paliperidone palmitate 3-month) following at least one 3-month injection cycle.

Lybalvi criteria:

Lybalvi: Step through aripiprazole and Latuda. If criteria is met then initial approval for 3 months. Subsequent approvals will be based on evidence of not gaining >= 10 % baseline body

weight for ongoing approval. If weight gain >= 10 % of initial body weight, then criteria for ongoing use not met.

Livtencity criteria:

Livtencity is a substrate of CYP3A4. Coadministration of Livtencity® with strong inducers of CYP3A4 is not recommended, except for selected anticonvulsants. Must show failure or contraindication to all the following ganciclovir, valganciclovir, cidofovir and foscarnet before Livtencity will be approved.

Board Decision: The Board unanimously approved the above recommendation.

NEW BUSINESS

INTRODUCE: OPIOID USE FROM MULTIPLE PROVIDER

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 patients. 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.

Per the Chapter 11 Rule of the Maine Legislature, Rules Governing the Controlled Substances Prescription Monitoring Program and Prescription of Opioid Medications, pharmacy requirements also exist to help prevent opioid misuse. Pharmacists must review:

1. the aggregate MMEs for the patient.
2. the number of prescribers currently prescribing any controlled substances to the patient.
3. the number of pharmacies currently filling controlled substance prescriptions for the patient.
4. if the patient is from out of state.
5. if the patient pays cash.
6. if there are no opioids prescribed in the past 12 months.

The pharmacist is expected to decline filling the prescription until contact is made with the prescriber to communicate concerning information and verify that the prescriber still wants to prescribe the medication. 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. We will use paid, non-reversed Medicaid pharmacy claims from calendar year 2021, excluding members with Part D, MaineRX and TPL. We 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 Maine Medicaid. It will not include cash prescriptions. For those with multiple prescribers we will look to see if there was dose escalation and if any of the prescriptions overlapped.

Board Decision: None at this time

PRESENTATION: CONCURRENT USE OF GPL-1 RECEPTOR AGONISTS, DPP-4 INHIBITORS

Treatment for Type 2 DM has improved substantially in the last decade. Several effective classes of medications are now available, including glucagon-like peptide-1 receptor agonists (GLP-1 agonists), sodium-glucose co-transporter 2 inhibitors (SGLT-2 inhibitors) and dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors, also called gliptins), along with older medications, such as sulfonylureas and insulin. Recent guidelines from the American Diabetes Associate and the American Society of Endocrinology incorporate these newer agents into treatment algorithms, often recommending considering these drugs before starting insulin therapy. Some of these agents have beneficial effects on other risks, such as heart failure and other cardiovascular diseases and determining which drugs to use depends on an individual's health profile. GLP-1 receptor agonists work by stimulating insulin secretion and decreasing glucagon production. DPP-4 inhibitors prevent the degradation of GLP-1. Both have shown benefit in lowering blood glucose, however comparative trials have shown GLP-1 receptor agonists to be superior in improving glycemic control and inducing weight loss. Studies have shown that combining a GLP-1 agonist with a DPP-4 inhibitor provides minimal improvement in glycemic control and weight loss compared with either monotherapy and is not cost effective. Guidelines do not support combined therapy with these drugs. We looked at all members with a diagnosis of Type II DM to identify if any are being prescribed both a DDP-4 inhibitor and GLP-1 agonist to determine if the practice is widespread or isolated among a few providers. This will determine if there should be adjustment to the PDL, PA process or if provider education is warranted.

Recommendation: Most of the members were not on overlapping prescriptions and many who were on them took them together for a relatively short period of time, likely a transition phase from one drug to another. Only 49 members were on both for more than 180 days. Given the large number of potential prescribers of medications to treat diabetes, a general educational reminder might be in order. Alternatively, identification of the prescribers who have members on both medications for more than 180 days would allow for a more targeted educational approach. It is a bit concerning that some members are getting their diabetes medications from completely different prescribers for all claims filed. An analysis of that cohort of members/claims might also be helpful to explain why that is happening, as it could be dangerous if each prescriber is unaware of the other.

Board Decision: After board discussion it was decided that Change Healthcare would look into the prescriber's specialty and if it is primarily primary care providers prescribing then a targeted educational mailing could be done.

NEW DRUG REVIEW

Camcevi® (Leuprolide); **PDL category-** Cancer

Leuprolide mesylate, the active ingredient of Camcevi®, is a synthetic nonapeptide analog of naturally occurring gonadotropin-releasing hormone (GnRH) and is a GnRH agonist. It acts as an inhibitor of gonadotropin secretion. Animal and human studies indicate that following an initial stimulation of gonadotropins, chronic administration of leuprolide results in suppression of ovarian and testicular steroidogenesis. This effect is reversible upon discontinuation of drug therapy. In humans, subcutaneous (SC) administration of leuprolide results in an initial increase of circulating levels of luteinizing hormone (LH)

and follicle stimulating hormone (FSH), leading to a transient increase in levels of the gonadal steroids (testosterone and dihydrotestosterone in males); however, continuous daily administration of leuprolide results in decreased levels of LH and FSH. In males, testosterone is reduced to below castration levels. These decreases generally occur within 2 to 4 weeks after initiation of treatment, and castration levels of testosterone in prostatic cancer patients have been demonstrated for periods of up to 5 years. It is indicated for the treatment of adult patients with advanced prostate cancer. The efficacy of Camcevi® was assessed in an open-label, single-arm, multinational study that included patients with advanced prostate carcinoma who had a baseline morning serum testosterone level >150ng/dL and an Eastern Cooperative Oncology Group performance status ≤2. In the clinical trial, PSA levels were monitored and were lowered on average by 51% after 4 weeks after Camcevi® administration, 83% after 3 months and remained suppressed throughout the 48 weeks of treatment. These PSA results should be interpreted with caution because of the heterogeneity of the patient population studied. No evidence has shown that the rapidity of PSA decline correlates with clinical benefit. he efficacy of Camcevi® was assessed in an open-label, single-arm study that included a population with a median age of 71 years. The main efficacy outcome measure was medical castration rate, defined as achieving and maintaining serum testosterone suppression to ≤50ng/dL by week 4 through week 48 of treatment. After the first injection of Camcevi®, serum testosterone levels were suppressed to ≤50ng/dL by week 4 in 98.5% of patients and from week 4 through 48 in 97% of patients.

Recommendation: Camcevi® to non-preferred.

Cibinqo® (abrocitinib); **PDL category-** Topical- Atopic Dermatitis

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. Treatment with Cibinqo® was associated with dose-dependent reduction in serum markers of inflammation, including high sensitivity C-reactive protein (hsCRP), interleukin-31 (IL-31), and thymus and activation regulated chemokine (TARC). These changes returned to near baseline within 4 weeks of drug discontinuation. 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.)

Recommendation: Cibingo® to non-preferred.

Clinical Criteria: Adbry and Cibinqo: Preferred drugs also indicated for this condition, including topical steroids, cyclosporin AND calcineurin inhibitors must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists. Additionally, after trials above approvals would be granted for Mild Atopic Dermatitis: 1. Eucrisa, 2.

Opzelura. For Moderate Atopic Dermatitis: 1. Dupixent, 2. Rinvoq. For Moderate/Severe Atopic Dermatitis: 1. Dupixent, 2. Rinvoq Note: If unable to use TCIs then a trial of Eucrisa could be recommended before Dupixent.

Dartisla® (glycopyrrolate ODT); **PDL category**- GI- Anti-diarrheal/Antacid, Miscellneous

Glycopyrrolate, the active ingredient of Dartisla® ODT, is an anticholinergic (antimuscarinic) agent. It inhibits the action of acetylcholine on parietal cells in the stomach and decreases the volume and acidity of gastric secretions. It is indicated in adults to reduce symptoms of a peptic ulcer as an adjunct to treatment of peptic ulcer. It is not indicated as monotherapy for treatment of peptic ulcer because effectiveness in peptic ulcer healing has not been established. There were no clinical trials identified in the prescribing information for Dartisla® ODT. Glycopyrrolate tablets, available as 1mg and 2mg tablets, have been available for numerous years and have been found to be safe and effective. They have the same indication as Dartisla® OTD. After Dartisla® ODT 1.7mg administration, the AUC and Cmax of glycopyrrolate were comparable to an oral 2mg glycopyrrolate tablet. Glycopyrrolate tablets (1mg and 2mg) have been available for several years and have the same indication as Dartisla® ODT. Dartisla® ODT offers prescribers a different dosage form.

Recommendation: Dartisla ODT® to non-preferred.

Clinical Criteria:

- It is not indicated as monotherapy for treatment of peptic ulcer because effectiveness in peptic ulcer healing has not been established.

Fleqsuvy® (baclofen oral suspension) **PDL category-** Muscle Relaxants

Baclofen, the active ingredient of Fleqsuvy®, is a gamma-aminobutyric acid (GABA-ergic) agonist. While the exact mechanism of action is not fully understood, baclofen inhibits both monosynaptic and polysynaptic reflexes at the spinal level, possibly by decreasing excitatory neurotransmitter release from afferent terminals, although actions at supraspinal sites may also occur and contribute to its clinical effect. Baclofen is a structural analog of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) and may exert its effects by stimulation of the GABA-B receptor subtype. Baclofen has been shown to have general CNS depressant properties, as indicated by the production of sedation with tolerance, somnolence, ataxia, and respiratory and cardiovascular depression. It is indicated for the treatment of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity. Fleqsuvy® may also be of some value in patients with spinal cord injuries and other spinal cord diseases. It is not indicated in the treatment of skeletal muscle spasm resulting from rheumatic disorders. There are no clinical trials in the prescribing information for Fleqsuvy®. The efficacy of Fleqsuvy® is based upon a bioavailability study in healthy adults comparing baclofen oral tablets to Fleqsuvy®. A pharmacokinetic study in healthy adult male and female subjects under fasting conditions at a 20mg dose level demonstrated similar bioavailability for baclofen oral suspension and oral tablets. Baclofen oral tablets have been available for numerous years and have the same indication as Fleqsuvy®. Fleqsuvy® offers providers a treatment option in a different dosage formulation.

Recommendation: Fleqsuvy® XR to non-preferred.

Ibsrela® (tenapanor); **PDL category**- GI- Miscellaneous

Tenapanor, the active ingredient of Ibsrela®, is a locally acting inhibitor of the sodium/hydrogen exchanger 3 (NHE3), an antiporter expressed on the apical surface of the small intestine and colon mainly responsible for the absorption of dietary sodium. In vitro and animal studies indicate its major metabolite (M1) is not active against NHE3. By inhibiting NHE3 on the apical surface of the enterocytes, tenapanor reduces absorption of sodium from the small intestine and colon, resulting in an increase in water secretion into the intestinal lumen, which accelerates intestinal transit time and results in a softer stool consistency. It is indicated for the treatment of irritable bowel syndrome with constipation (IBS-C) in adults. he safety and efficacy of Ibsrela® were assessed in two double-blind, placebo-controlled, randomized, multicenter trials that included adult patients with IBS-C (Trial 1 and Trial 2). his product does have a box warning regarding the risk of serious dehydration in pediatric patients. The warning adds that use is contraindicated in patients less than 6 years of age and should be avoided in patients 6 years to less than 12 years of age. Furthermore, the safety and efficacy of use have not been established in the pediatric population less than 18 years of age. In 2 double-blind, placebo-controlled, phase 3 studies, there were more CSBM responders and abdominal pain responders in those treated with Ibsrela® as compared with placebo. Per the full-text study by Chey et al2 (Trial 1), a significantly greater proportion in the tenapanor treatment group were 6/12-week combined responders as compared with placebo ($p<0.001$). Per the full-text study by Chey et al3 (Trial 2), a significantly greater proportion treated with tenapanor met the primary endpoint than placebo ($p=0.020$). Head-to-head comparator studies with other active agents with the same indication were not identified.

Recommendation: Ibsrela® to non-preferred.

Clinical Criteria:

- Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists. Certain drugs require specific diagnoses for approval.

Kimmtrak® (tebentafusp-tebn); **PDL category**- Cancer

Tebentafusp-tebn, the active ingredient of Kimmtrak®, is a bispecific gp100 peptide-HLA-A*02:01 directed T-cell receptor CD3 T- cell engager. The TCR arm binds to a gp100 peptide presented by human leukocyte antigen-A*02:01 (HLA-A*02:01) on the cell surface of uveal melanoma tumor cells. In vitro, tebentafusp-tebn bound to HLA-A*02:01-positive uveal melanoma cells and activated polyclonal T cells to release inflammatory cytokines and cytolytic proteins, which results in direct lysis of uveal melanoma tumor cells. It is indicated for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma. The efficacy of Kimmtrak® was assessed in a randomized, open-label, multicenter study (IMCgp100-202) that enrolled patients with metastatic uveal melanoma (N=378). Patients were required to be HLA-A*02:01 genotype positive identified by a central assay. Prior surgical resection of oligometastatic disease was permitted. Note that patients with clinically significant cardiac disease or the presence of symptomatic or untreated brain metastasis were excluded. Patients were also excluded if they received prior systemic therapy for metastatic or advanced uveal melanoma or localized liver-directed therapy. The main efficacy outcome was overall survival, and the number of deaths was significantly fewer in the Kimmtrak® arm compared to the active comparator arm (NNT 7; $p<0.0001$).

Recommendation: Kimmtrak® to non-preferred.

Opdualag® (nivolumab and relatimab-rmbw); **PDL category**- Cancer

Nivolumab and relatlimab-rmbw, the active ingredients of Opdualag®, is a fixed-dose combination of two IgG4 kappa monoclonal antibodies (mAbs). Nivolumab is a programmed death receptor-1 (PD-1) blocking antibody while relatlimab-rmbw is a lymphocyte activation gene-3 (LAG-3) blocking antibody. Relatlimab-rmbw binds to the LAG-3 receptor, blocks interaction with its ligands, and reduces LAG-3 pathway-mediated inhibition of the immune response. Antagonism of this pathway promotes T cell proliferation and cytokine secretion. It is indicated for the treatment of adult and pediatric patients 12 years of age or older with unresectable or metastatic melanoma. The efficacy of Opdualag® was assessed in a randomized, double-blind trial (N=714) that included patients with previously untreated metastatic or unresectable Stage III or IV melanoma. The efficacy of Opdualag® was assessed in a double-blind, active-comparator study that included previously untreated metastatic or unresectable Stage III or IV melanoma patients (N=714). Results of this trial demonstrated a statistically significant improvement in progression free survival for patients randomized to Opdualag® compared with the nivolumab group. The final analysis of overall survival was not statistically significant.

Recommendation: Opdualag ® to non-preferred.

Pyrukynd® (mitapivat); **PDL category**- Pyruvate Kinase Deficiency Agents

Mitapivat, the active ingredient of Pyrukynd®, is a pyruvate kinase activator that acts by allosterically binding to the pyruvate kinase tetramer and increasing pyruvate kinase (PK) activity. The red blood cell (RBC) form of pyruvate kinase (PK-R) is mutated in PK deficiency, which leads to reduced adenosine triphosphate (ATP), shortened RBC lifespan, and chronic hemolysis. It is indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency. The efficacy of Pyrukynd® was assessed in a multinational, randomized, double-blind, placebo-controlled study (ACTIVATE) that included adults with PK deficiency (N=80) who were not regularly transfused, defined as having had no more than 4 transfusions in the 52-week period prior to treatment and no transfusions in the 3-month period prior to treatment. One small study assessed the efficacy of Pyrukynd® as compared with placebo in patients with PK deficiency not regularly transfused. Efficacy was based on Hb response, and statistically significantly more subjects in the Pyrukynd® group had a Hb response as compared with placebo (NNT 3, calculated by CHC). A second small study assessed the efficacy of Pyrukynd® in patients with PK deficiency who were regularly transfused. Efficacy was based on transfusion reduction response and 33% of study subjects met this primary endpoint. In addition, 22% were transfusion free. One noted reference source noted that "…it would be reasonable to try mitapivat in any individual with PK deficiency who requires transfusion." Furthermore, it is noted that "mitapivat may also be reasonable in individuals with symptomatic anemia who do not require transfusions, and even in individuals with compensated hemolysis who do not have overt anemia…". Overall the authors suggest mitapivat for adults with PK deficiency with symptomatic anemia (transfusion-dependent or not requiring transfusions). It is recommended that Pyrukynd® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

Recommendation: Pyrukynd® to non-preferred.

Seglentis® (celecoxib/tramadol HCl); **PDL category**- Narcotics- Selected

Seglentis® is a combination product containing celecoxib (a NSAID) and tramadol (an opioid agonist and inhibitor of norepinephrine and serotonin reuptake). Celecoxib is an analgesic with anti-inflammatory and antipyretic properties. The mechanism of action is believed to be due to inhibition of prostaglandin

synthesis, primarily via inhibition of COX-2. While the mode of action of tramadol is not completely understood, the analgesic effect is believed to be due to both binding to μ-opioid receptors and weak inhibition of reuptake of norepinephrine and serotonin. Seglentis® is a Schedule IV controlled substance. Tramadol is a substance with a high potential for abuse similar to other opioids and can be abused and is subject to misuse, addiction, and criminal diversion. Both tolerance and physical dependence can develop during opioid therapy. It is indicated for the management of acute pain in adults that is severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Seglentis® 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 and have not provided adequate analgesia or are not expected to provide adequate analgesia. The safety and efficacy of Seglentis® were assessed in a randomized, double-blind, parallel group study comparing Seglentis® to tramadol, celecoxib, and placebo that included adults (N=637) that were 18 years of age or older (age ranged from 18 and 77 years) with acute post-operative pain (≥5 and ≤9 on a 0-10 Numeric Pain Rating Scale [NPRS]) following unilateral first metatarsal osteotomy with internal fixation. Patients were randomized to Seglentis® 200mg BID, tramadol 50mg Q6H, celecoxib 100mg BID, or placebo in a double-blind, double-dummy manner. Use of rescue medication (acetaminophen and oxycodone) was permitted during the study. Seglentis® has a box warning with numerous increased risks. In one double-blind, double-dummy study that compared Seglentis® with tramadol, celecoxib, and placebo, results suggested that Seglentis® had statistically significantly better mean SPID48 scores (primary endpoint) as compared with placebo or either of the individual ingredients of Seglentis®.

Recommendation: Seglentis® to non-preferred.

Clinical criteria:

- Only available if component ingredients are unavailable.

Tarpeyo® (budesonide capsule, delayed release) **PDL category**- Hematological Agent- IgAN

Budesonide, the active ingredient of Tarpeyo®, is a synthetic corticosteroid with potent glucocorticoid activity and weak mineralocorticoid activity that undergoes substantial first pass metabolism. Mucosal B-cells present in the ileum, including the Peyer's patches, express glucocorticoid receptors and are responsible for the production of galactose-deficient IgA1 antibodies (Gd-Ag1) causing IgA nephropathy. Through their anti-inflammatory and immunosuppressive effects at the glucocorticoid receptor, corticosteroids can modulate B-cell numbers and activity. It has not been established to what extent the efficacy of Tarpeyo® is mediated vial local effects in the ileum vs systemic effects. It is indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5g/g. This indication is approved under accelerated approval based on a reduction in proteinuria. It has not been established whether Tarpeyo® slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial. The effect of Tarpeyo® on proteinuria was assessed in a randomized, double-blind, multicenter study that included patients with biopsy-proven IgAN, eGFR ≥35ml/min/1.73m2, and proteinuria (defined as either ≥1g/day or UPCR ≥0.8g/g) who were on a stable dose of maximally-tolerated RAS inhibitor therapy. In a double-blind study, the Tarpeyo® group had a 34% reduction in UPCR at 9 months compared to baseline while the placebo group had a 5% reduction in UPCR. This result was statistically significant in favor of Tarpeyo®.

Recommendation: Add new PDL category Hematological Agents-IgAN. Tarpeyo® to non-preferred.

Clinical Criteria:

- PA required to confirm FDA approved indication.

Tivdak® (tisotumab vedotin-tftv); **PDL category**- Cancer

Tisotumab vedotin-tftv, the active ingredient of Tivdak®, is a Tissue Factor (TF) directed antibody drug conjugate (ADC) comprised of a human anti-TF IgG1-kappa antibody conjugated to the microtubule-disrupting agent monomethyl auristatin E (MMAE) via a protease-cleavable vc (valine-citrulline) linker. The antibody is a human IgG1 directed against cell surface TF. TF is the primary initiator of the extrinsic blood coagulation cascade. The small molecule, MMAE, is a microtubule-disrupting agent, attached to the antibody via a protease-cleavable linker. Nonclinical data suggests that the anticancer activity of tisotumab vedotin-tftv is due to the binding of the ADC to TF expressing cancer cells, followed by internalization of the ADC-TF complex, and release of MMAE via proteolytic cleavage. MMAE disrupts the microtubule network of actively dividing cells, leading to cell cycle arrest and apoptotic cell death. In vitro, tisotumab vedotin-tftv also mediates antibody-dependent cellular phagocytosis and antibody-dependent cellular cytotoxicity. It is indicated for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The efficacy of Tivdak® was assessed in an open-label, multicenter, single-arm trial that included patients with recurrent or metastatic cervical cancer who had received no more than 2 prior systemic regimens in the recurrent or metastatic setting, including at least one prior platinum-based chemotherapy regimen. The primary efficacy outcome of confirmed objective response rate was 24%.

Recommendation: Tivdak® to non-preferred.

Twyneo® (trtinoin & benzoyl peroxide cream); **PDL category**- Topical- Acne preroxide cream

Twyneo® cream is a combination of tretinoin and benzoyl peroxide. Tretinoin is a retinoid and benzoyl peroxide is an oxidizing agent. It is indicated for the topical treatment of acne vulgaris in adults and pediatric patients 9 years of age and older. The safety and efficacy of Twyneo cream® were assessed in two randomized, double-blind, multicenter, vehicle-controlled trials of identical design that included subjects 9 years of age and older with facial acne vulgaris (N=858). Patients were treated once daily with either Twyneo® cream or vehicle for 12 weeks. Subjects were required to have a score of moderate (3) or severe (4) on the Investigator Global Assessment (IGA), 20 to 100 inflammatory lesions (papules, pustules, and nodules), 30 to 150 non-inflammatory lesions (open and closed comedones) and two or fewer facial nodules. Treatment success at week 12 (one of the co-primary efficacy endpoints) was obtained more frequently with Twyneo® than vehicle (NNT of 4 for study 1 and NNT of 9 for study 2). Comparator studies with active ingredients were not found.

Recommendation: Twyneo® to non-preferred.

Vabysmo® (faricimab- svoa); **PDL category**- Op- Of Interest

Faricimab-svoa, the active ingredient of Vabysmo®, is a humanized bispecific immunoglobulin G1 (IgG1) antibody that binds to both vascular endothelial growth factor A (VEGF-A) and angiopoietin-2 (Ang-2). It is a humanized bispecific antibody that acts through inhibition of two pathways by binding to VEGF-A and

Ang-2. By inhibiting VEGF-A, faricimab suppresses endothelial cell proliferation, neovascularization, and vascular permeability. By inhibiting Ang-2, faricimab is thought to promote vascular stability and desensitize blood vessels to the effects of VEGF-A. Ang-2 levels are increased in some patients with nAMD and DME (see below). The contribution of Ang-2 inhibition to the treatment effect and clinical response for nAMD and DME has yet to be established. It is indicated for the treatment of patients with Neovascular (wet) Age-Related Macular Degeneration (nAMD) and Diabetic Macular Edema (DME). The safety and efficacy of Vabysmo® were assessed in 2 randomized, multicenter, double-masked, active-comparator controlled, identically-designed 2-year studies in patients with nAMD. In both studies, Vabysmo® treated patients had a non-inferior mean change from baseline in BCVA compared to patients treated with aflibercept. In all studies, results demonstrated non-inferiority of Vabysmo® to the comparator control (aflibercept) for the primary endpoint, defined as the mean change from baseline in BCVA at year 1 (when averaged over the week 40, 44, and 48 visits in study 1; and the average of week 48, 52, and 56 visits in study 2), measured by the ETDRS Letter Score.

Recommendation: Vabysmo® to non-preferred.

Vijoice® (alpelisib); **PDL category**- PROS Agents

Alpelisib, the active ingredient of Vijoice®, is a kinase inhibitor. It is an inhibitor of phosphatidylinositol-3-kinase (PI3K) with inhibitory activity predominantly against PI3Kα. Gain-of-function mutations in the gene encoding the catalytic α-subunit of PI3K (PIK3CA) lead to activation of PI3Kα and Akt-signaling, cellular transformation, and the generation of tumors in in vitro and in vivo models. It is indicated for the treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA-Related Overgrowth Spectrum (PROS) who require systemic therapy. It is indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). The efficacy of Vijoice® was assessed in EPIK-P1, a single-arm clinical study that included patients who were treated as part of an expanded access program for compassionate use which enrolled patients across 7 sites in 5 countries (France, Spain, US, Ireland, and Australia). The major efficacy outcome, the proportion of patients with radiological response at week 24, was 27%. It is recommended that Vijoice® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

Recommendation: Vijoice® to non-preferred.

Clinical Criteria:

- PA required to confirm FDA approved indication.

Xipere® (triamcinolone acetonide injection, suspension); **PDL category**- OP- Anti-inflammatory/Steroids Op.

Triamcinolone acetonide, the active ingredient of Xipere®, is a synthetic glucocorticoid (glucocorticoids are often referred to as corticosteroids) with immunosuppressive and anti-inflammatory activity. The primary mechanism of action is as a corticosteroid hormone receptor agonist. It is indicated for the treatment of macular edema associated with uveitis. The safety and efficacy of Xipere® were assessed in a 6-month, randomized, multicenter double-masked, sham-controlled study that included patients with macula edema associated with anterior-, intermediate-, posterior-, or pan-uveitis. Patients were treated at baseline and week 12. Results suggested that significantly more in the Xipere® group achieved the primary outcome as compared with the control.

Recommendation: Xipere® to non-preferred.

Zimhi® (naloxone HCl injection); **PDL category-** Narcotic- Antagonists

Naloxone, the active ingredient of Zimhi®, is an opioid antagonist that antagonizes opioid effects by competing for the same receptor sites. Naloxone reverses the effects of opioids, including respiratory depression, sedation, and hypotension. Also, it can reverse the psychotomimetic and dysphoric effects of agonist-antagonists such as pentazocine. It is indicated in adults and pediatric patients for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or CNS depression. Zimhi® is intended for immediate administration as emergency therapy in settings where opioids may be present. It is not a substitute for emergency medical care. There are no clinical trials in the Zimhi® prescribing information. Zimhi® was approved through the 505(b)(2) pathway, and this pathway "…may rely on the FDA's finding that a previously approved drug is safe and effective or on published literature to support the safety and/or effectiveness of the proposed product…".2 Per an FDA bulletin, the "…manufacturer submitted a 505(b)(2) application that relied, in part, on the FDAs finding of safety and effectiveness for naloxone hydrochloride (Narcan® injection) to support approval."2 Generic naloxone injections are currently available; however, per a small study with healthy adults (N=14), a single 5mg IM injection of Zimhi® in a single-dose, prefilled syringe in a delivery device provides significantly higher Cmax and AUC as compared to a single IM injection of 2mg naloxone (1mg/1ml). There is no evidence at this time to support that Zimhi® is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Zimhi® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

Recommendation: Zimhi® to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

None at this time

Board Decision: No action.

ADJOURNMENT: 8:30PM

The next meeting will be held on **September 13, 2022** 530pm- 8:30pm virtually.