Washington Pharmacy Advisory Committee Meeting

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Agenda Topics

- Overview of Disease State
- Indications
- Dosage & Formulations
- Guideline Updates

Antidepressants, Other

ANTIDEPRESSANTS : GABA RECEPTOR MODULATOR - NEUROACTIVE STEROID

Antidepressants, Other – Disease State Description

Perinatal Depression

❖ American Congress of Obstetricians and Gynecologists (ACOG), 2023

- First line pharmacotherapy for the treatment of perinatal depression: SSRIs
- If successfully treated previously with an antidepressant from any class, this should be the agent of choice
- Untreated depression during pregnancy is associated with disrupted health behaviors, relationships, parenting, and physiology
- Risks and benefits of psychopharmacotherapy for perinatal mental health conditions should be discussed with the patient when clinically indicated
- ACOG clinical practice guidelines do not address the role of zuranolone (Zurzuvae) in the management of postpartum depression (PPD)

Antidepressants, Other

Zurzuvae (zuranolone)

- **August 2023 - FDA approved a neuroactive steroid GABA-A receptor positive modulator as the first oral treatment indicated to treat postpartum depression (PPD) in adults**
  - **Schedule IV controlled substance under the Controlled Substances Act**
- **FDA Indication**
  - **Treatment of PPD in adults**
- **Warnings**
  - **BBW: Impaired ability to drive or engage in other potentially hazardous activities**
  - **Suicidal Thoughts and Behavior: Consider changing the therapeutic regimen, including discontinuing, in patients whose PPD worsens, or who experience emergent suicidal thoughts and behaviors**
  - **Embryo-fetal Toxicity: Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for one week after the final dose**
- **Dosage**
  - **Can be used alone or as an adjunct to oral antidepressant treatment**
  - **Recommended dosage: 50 mg orally once daily in the evening with a fatty meal for 14 days**
  - **Central Nervous System (CNS) depressant effects: May reduce dose to 40 mg once daily**
  - **Severe hepatic impairment & moderate or severe renal impairment: Reduce dose to 30 mg once daily**
- **Availability**
  - **Oral capsules: 20 mg, 25 mg, and 30 mg**

Antiparkinson’s Agents

ANTIPARKINSON AGENTS : ADENOSINE RECEPTOR ANTAGONISTS

ANTIPARKINSON AGENTS : DOPAMINERGICS

ANTIPARKINSON AGENTS : MONOAMINE OXIDASE INHIBITORS (MAOI)

Antiparkinson's Agents

New Generic

❖ **safinamide – July 2023**

- FDA approved the first generic for Xadago (safinamide) tablets by Aurobindo

Discontinuation

❖ **Mirapex ER (pramipexole ER) – August 2023**

- FDA is reporting discontinuation of Mirapex ER by Boehringer Ingelheim; generics remain

Bile Salts

GASTROINTESTINAL AGENTS : ILEAL BILE ACID TRANSPORTER INHIBITORS

Bile Salts – Disease State Description

Pruritis Associated with Alagille syndrome (ALGS) or Progressive Familial Intrahepatic Cholestasis (PFIC)

- Alagille syndrome is an inherited condition that causes a build-up of bile in the liver due to lack of adequate numbers of bile ducts to drain the bile, which leads to liver damage
  - Signs and symptoms include severe itchy skin related to the presence of bilirubin as well as jaundice, delayed growth, xanthomas, heart murmur, vascular changes, distinct facial features, kidney disease, and enlarged spleen
- Progressive familial intrahepatic cholestasis is characterized by an itch that is disabling and includes the eyes and ears
- Agents approved for use in patients with pruritis resulting from either Alagille syndrome or progressive familial intrahepatic cholestasis are: maralixibat (Livmarli) and odevixibat (Bylvay)

Bile Salts

Livmarli (maralixibat)

- **March 2024 - FDA approved for treatment of cholestatic pruritus in patients ≥ 5 years old with progressive familial intrahepatic cholestasis (PFIC)**
- **FDA Indications**
  - Treatment of cholestatic pruritus in patients 3 months of age and older with Alagille syndrome (ALGS)
  - **Treatment of cholestatic pruritus in patients 5 years of age and older with PFIC**
    - **Limitation of use: Not recommended in a subgroup of PFIC type 2 patients with specific ABCB11 variants resulting in non-functional or complete absence of bile salt export pump (BSEP) protein**
- **Warnings**
  - **Contraindicated: Prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy)**
  - Hepatotoxicity
  - Gastrointestinal Adverse Reactions
  - Fat-Soluble Vitamin Deficiency
- **Dosage**

Indication	Recommended Dose	Starting Dose	Titration	Maximum daily dose
ALGS	380 mcg/kg once daily, taken 30 minutes before a meal in the morning	190 mcg/kg orally once daily	Increase to 380 mcg/kg once daily after one week, as tolerated	28.5 mg
PFIC	**570 mcg/kg twice daily, taken 30 minutes before a meal**	**285 mcg/kg orally once daily in the morning**	**Increase to 285 mcg/kg twice daily, 428 mcg/kg twice daily, and then to 570 mcg/kg twice daily, as tolerated**	**38 mg**

- **Availability**
  - Oral solution: 9.5 mg of maralixibat per mL

Ophthalmics, Glaucoma Agents

GLAUCOMA AGENTS : ADRENERGIC AGENTS

GLAUCOMA AGENTS : ADRENERGIC AGENTS COMBINATIONS

GLAUCOMA AGENTS : BETA - BLOCKERS

GLAUCOMA AGENTS : BETA - BLOCKERS COMBINATIONS

GLAUCOMA AGENTS : CARBONIC ANHYDRASE INHIBITORS

GLAUCOMA AGENTS : KINASE INHIBITORS

GLAUCOMA AGENTS : MIOTICS

GLAUCOMA AGENTS : PROSTAGLANDINS

Ophthalmics, Glaucoma Agents – Disease State Description

Glaucoma

- Approximately 3 million people in the United States (US) suffer from glaucoma
- Second most common cause of permanent blindness in the US
- Leading cause of blindness among Hispanics and the second most common cause of blindness among African Americans
- Increased intraocular pressure (IOP) is common in glaucoma and is believed to contribute to the damage to the optic nerve, which can lead to loss of visual sensitivity and field
  - Some patients with glaucoma have normal IOP, and many patients with elevated IOP do not develop glaucoma
  - IOP alone is no longer considered a diagnostic criterion for glaucoma
- Two major types of glaucoma: open-angle and closed-angle
  - Open-angle glaucoma: reduced flow through the trabecular meshwork and accounts for the majority of cases
  - Closed-angle glaucoma: the iris is pushed forward against the trabecular meshwork, blocking fluid from escaping
- Presbyopia is an age-related gradual loss of near focusing ability of the eye due to the loss of elasticity of the lens
- **American Academy of Ophthalmology (AAO), 2020**
  - Prostaglandin analogs are the most frequently prescribed eye drops to lower IOP due to their efficacy, safety profile, and once-daily regimen
  - Sufficient management of glaucoma is dependent on a high level of adherence to therapy
  - Data has suggested the addition of a second medication can lead to reduced adherence; therefore, fixed-dose combinations may potentially increase adherence and decrease exposure to preservatives
  - Although fixed-dose combinations are not usually recommended as initial therapy, a fixed-dose combination agent may be warranted in patients requiring a greater IOP reduction than available with a single agent

Ophthalmics, Glaucoma Agents

Qlosi (pilocarpine)

- October 2023 - FDA approved a cholinergic agonist, indicated for treatment of presbyopia in adults
- FDA Indications
  - Treatment of presbyopia in adults
- Warnings
  - Blurred Vision: Advise patients to not drive or operate machinery if vision is not clear
  - Risk of Retinal Detachment: Examination of the retina is advised in all patients prior to initiation of therapy. Advise patients to seek immediate medical care with sudden onset of flashes of lights, floaters, or vision loss
  - Iritis: Caution is advised in patients with iritis
- Dosage
  - Instill 1 drop in each eye, can be repeated a second time after 2 to 3 hours for an effect up to 8 hours
  - Can be used daily or as needed, up to twice each day
- Availability
  - Ophthalmic solution: pilocarpine hydrochloride 0.4% (4 mg/mL) in a single-patient-use vial

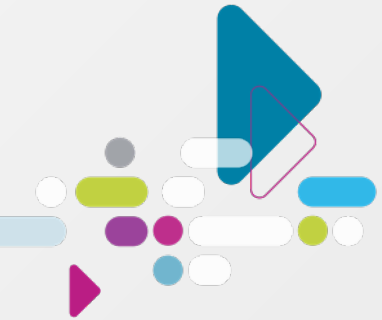
Ophthalmics, Glaucoma Agents

iDose TR (travoprost intracameral implant)

- **December 2023 - FDA approved prostaglandin analog indicated for the reduction of intraocular pressure (IOP) in patients with ocular hypertension (OHT) or open-angle glaucoma (OAG)**
- **FDA Indications**
  - **Reduction of IOP in patients with OHT or OAG**
- **Warnings**
  - **Iridocorneal Angles: Use caution in patients with narrow angles or other angle abnormalities**
  - **Device Dislocation: Monitor patients routinely to confirm the location of the iDose TR at the site of administration**
  - **Increased Iris Pigmentation: Iris pigmentation is likely to be permanent**
- **Dosage**
  - **Ophthalmic intracameral administration: 75 mcg implant for use as a single administration per eye**
    - **Administered under standard aseptic conditions by Health Care Practitioner**
    - **Should not be readministered to an eye that received a prior iDose TR**
- **Availability**
  - **Intracameral implant containing 75 mcg travoprost, pre-loaded in a single-dose inserter**

Paroxysmal Nocturnal Hemoglobinuria (PNH) Agents; Immunomodulators, miscellaneous

HEMATOLOGICAL AGENTS - MISC : COMPLIMENT INHIBITORS - INJECTABLE



Paroxysmal Nocturnal Hemoglobinuria (PNH) Agents – Disease State Description

Neuromyelitis Optica Spectrum Disorder (NMOSD)

- Also known as Devic's disease
- Rare autoimmune, inflammatory central nervous system (CNS) syndrome involving the optic nerve, spinal cord, and brain stem
- An estimated prevalence of 0.37 to 10 cases per 100,000 persons
- NMOSD is more common in women than in men
- Proposed to primarily be mediated by B cells, and aquaporin-4 immunoglobulin G antibodies (AQP4-IgG) are likely involved in the pathogenesis of NMOSD because they bind to astrocytes in the CNS
  - This binding can trigger attacks, such as loss of vision, paralysis, nerve pain, and respiratory failure
- No clinical practice guidelines for the treatment of NMOSD in the US
  - In practice, the standard treatment for acute attacks involves steroids, such as high-dose IV methylprednisolone or plasma exchange for patients with severe symptoms
  - The chances of relapse and permanent disability are approximately 90%

Paroxysmal Nocturnal Hemoglobinuria (PNH) Agents

Ultomiris (ravulizumab-cwvz)

- **March 2024 - FDA approved a new indication for the treatment of adults with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin 4 (AQP4) antibody positive**
- **FDA Indications**
  - Treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH)
  - Treatment of adult and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA)
    - Limitations of Use: Not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)
  - Treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive
  - **Treatment of adult patients with NMOSD who are AQP4 antibody-positive**
- **Warnings**
  - BBW: Life-threatening meningococcal infections/sepsis have occurred in patients treated and may become rapidly life-threatening or fatal if not recognized and treated early
- **Dosage**
  - See Full Prescribing Information for instructions on dosage, preparation, and administration
  - Dilute vial before use and administer as an intravenous infusion through a 0.2 or 0.22 micron filter
  - **Recommended dosage is based on patient's body weight**
- **Availability**
  - Intravenous Injection: 300 mg/30 mL (10 mg/mL), 300 mg/3 mL (100 mg/mL), 1,100 mg/11 mL (100 mg/mL) solutions in a single-dose vial

Disease State Description

CD55-Deficient Protein-Losing Enteropathy (PLE)

- Also known as complement hyperactivation, angiopathic thrombosis, and protein-losing enteropathy (CHAPLE) disease
- Rare genetic disorder caused by a mutation in the gene encoding for complement decay-accelerating factor (CD55) combined with immunodeficiency
  - Mutations in the CD55 gene leads to the inability to control complement activity (a cascade of proteins that provides host defense) resulting in an overactive complement system that causes damage to the blood and lymph vessels in the digestive tract
- Patients have chronic abdominal and cardiovascular symptoms and can also experience severe recurrent infections as well as potentially fatal thrombosis
- Pozelimab-bbfg (Veopoz) is the first FDA approved treatment for CHAPLE disease

Drug Update

Veopoz (pozelimab-bbfg)

- August 2023 - FDA has approved a complement inhibitor as the first treatment for adult and pediatric patients ≥ 1 year old with CD55-deficient protein-losing enteropathy (PLE), also known as complement hyperactivation, angiopathic thrombosis, and protein-losing enteropathy (CHAPLE) disease
- FDA Indication
  - Treatment of adult and pediatric patients 1 year of age and older with CD55-deficient PLE, also known as CHAPLE disease
- Warnings
  - BBW: Life-threatening meningococcal infections/sepsis have occurred in patients treated and may become rapidly life-threatening or fatal if not recognized and treated early
  - Other Bacterial Infections: Interrupt treatment in patients undergoing treatment for a serious encapsulated bacterial infection until the infection is resolved
  - Systemic Hypersensitivity Reactions: Interrupt infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory comprise occur
- Dosage
  - Single 30 mg/kg IV loading dose on day 1, then 10 mg/kg SC once weekly starting on day 8 and thereafter
    - All doses must be administered by a Health Care Practitioner
    - Maintenance dose may be increased to 12 mg/kg SC once weekly if there is inadequate clinical response after at least 3 weekly doses; maximum weekly dose is 800 mg
- Availability
  - Injection: 400 mg/2 mL (200 mg/mL) in a single-dose vial

Immunomodulators, miscellaneous – Disease State Description

Myasthenia Gravis (MG)

- Relatively uncommon disorder but is the most common disorder of neuromuscular transmission and is caused by an antibody-mediated attack of the proteins in the postsynaptic membrane of the neuromuscular junction
- The cardinal feature of MG is fluctuating skeletal muscle weakness, often with true muscle fatigue
  - The fatigue is manifested by worsening contractile force of the muscle
- There are two clinical forms: ocular and generalized
  - Ocular myasthenia: weakness is limited to the eyelids and extraocular muscles
  - Generalized disease: weakness may also commonly affect ocular muscles, but it also involves a variable combination of bulbar, limb, and respiratory muscles
- There are four categories of therapies used to treat MG:
  1. Symptomatic treatment: anticholinesterase agents
  2. Chronic immunomodulating treatment: glucocorticoids and nonsteroidal immunomodulatory agents
  3. Rapid but transient immunomodulating treatment: plasmapheresis and intravenous immune globulin (IVIG)
  4. Surgical treatment: thymectomy
- **American Academy of Neurology, 2021**
  - International consensus guidance for the management of myasthenia gravis, updated in 2020, recommends methotrexate as a steroid-sparing option, rituximab as an option in AChR-Ab+ MG after failure of other agents, and eculizumab in severe, refractory, AChR-Ab+ gMG

Immunomodulators, miscellaneous

Zilbrysq (zilucoplan)

- October 2023 - FDA approved a complement inhibitor, indicated for treatment of generalized myasthenia gravis (gMG) in adults who are antiacetylcholine receptor (AChR) antibody positive
- FDA Indication
  - Treatment of gMG in adults who are AChR antibody positive
- Warnings
  - BBW: Serious meningococcal infections: Life-threatening meningococcal infections/sepsis have occurred in patients treated and may become rapidly life-threatening or fatal if not recognized and treated early
  - Pancreatitis and pancreatic cysts: Discontinue in patients with suspected pancreatitis and initiate appropriate management until pancreatitis is ruled out or has resolved
- Dosage
  - Subcutaneous based on patient's body weight ranging from 16.6 mg once daily to 32.4 mg once daily
- Availability
  - Single-dose prefilled syringes: 16.6 mg/0.416 mL, 23 mg/0.574 mL, or 32.4 mg/0.81 mL

Oncology, Oral – Hematologic, Breast, and Other

ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS - ORAL

Oncology, Oral – Other - Disease State Description

Colon Cancer

- In the United States, colon cancer is the third most diagnosed cancer, as well as the second leading cause of death from cancer in both men and women
- **National Comprehensive Cancer Network (NCCN) Guidelines, 2023**
  - Indicate both regorafenib (Stivarga) or trifluridine/tipiracil (Lonsurf) with or without bevacizumab (given at a dose of 5 mg/kg on days 1 and 15 of a 28-day cycle) are treatment options for patients who have progressed through all other standard regimens (category 2A for both)
  - Although the FDA-approved dose of regorafenib is 160 mg daily for 21 days of a 28-day cycle, the NCCN guidelines note it is common practice to start at a lower dose for the first cycle, giving 80 mg for the first 7 days followed by 120 mg daily on days 8 through 14, and then 160 mg daily on days 15 through 21

Oncology, Oral – Other

Lonsurf (trifluridine/tipiracil)

- **August 2023 - FDA approved for use in combination with bevacizumab for adults with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin- & irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy**
- **FDA Indication**
  - **Treatment of adult patients with metastatic colorectal cancer** as a single agent or **in combination with bevacizumab who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy**
  - Treatment of adult patients with metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy
- **Warnings**
  - Severe Myelosuppression: Obtain complete blood counts prior to and on Day 15 of each cycle. Withhold and resume at next lower recommended dose
  - Embryo-Fetal Toxicity: Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception
- **Dosage**
  - 35 mg/m^2 up to a maximum of 80 mg per dose (based on the trifluridine component) orally twice daily with food on Days 1 through 5 and Days 8 through 12 of each 28-day cycle until disease progression or unacceptable toxicity
  - Round dose to the nearest 5 mg increment
- **Availability**
  - Oral Tablets: 15 mg trifluridine/6.14 mg tipiracil or 20 mg trifluridine/8.19 mg tipiracil

Immunomodulators, Atopic Dermatitis

ATOPIC DERMATITIS AGENTS : IMMUNOSUPPRESSIVE AGENTS - TOPICAL COMBINATIONS

Pompe Disease

ENDOCRINE AND METABOLIC AGENTS : GAA DEFICIENCY AGENTS

Mucopolysaccharidosis

ENDOCRINE AND METABOLIC AGENTS : MUCOPOLYSACCHARIDOSIS AGENTS

Octreotides & Related Agents

ENDOCRINE AND METABOLIC AGENTS : SOMATOSTATIC AGENTS

Urea Cycle Disorders

ENDOCRINE AND METABOLIC AGENTS : UREA CYCLE DISORDER AGENTS - ORAL

Vasopressin Receptor Antagonists

ENDOCRINE AND METABOLIC AGENTS : VASOPRESSIN RECEPTOR ANTAGONISTS - ORAL

Immunomodulators, Lupus

NEUROMUSCULAR AGENTS : SYSTEMIC LUPUS ERYTHEMATOSUS AGENTS

Oncology, Oral Other

ONCOLOGY AGENTS : METHYLTRANSFERASE INHIBITORS