Washington State Drug Utilization Review Board Meeting

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Washington State Health Care Authority

Antiparasitics: Folic Acid Antagonists

As of 06/2024 has combined with ANTIPARASITICS : ANTIMALARIALS drug class

Washington State Health Care Authority

Products Affected

- Pyrimethamine (Daraprim) 25 mg tablets
- ANTIPARASITICS : ANTIMALARIALS is an archived drug class on the AHPDL
- No motion or review needed for this drug class

Ophthalmic Agents:

Ectoparasiticides

Washington State Health Care Authority

Disease State Overview

- Blepharitis is a chronic ophthalmologic condition which is characterized by inflammation of the eyelid margin associated with eye irritation
- Classified as either posterior or anterior
  - Posterior
    - Most common type
    - Inflammation of the inner portion of the eyelid at the level of the meibomian glands
  - Anterior
    - Inflammation at the base of the eyelashes
- Dry eye disease is a common complication of blepharitis

Disease State Overview

- Symptoms
  - Red, swollen, itchy eyelids
  - Gritty or burning sensation
  - Pink eyes
  - Excessive tearing
  - Crusting or matting of eyelashes in the morning
  - Flaking or scaling of the eyelid skin
  - Light sensitivity
  - Blurred vision

Disease State Overview

- Management
  - Mild to moderate symptoms
    - Warm compresses, lid massage, lid washing, eye lubricants
  - Severe or continuing symptoms
    - Topical or oral antibiotic therapy + symptomatic measures
    - Topical ophthalmic antibiotic ointment is preferred (e.g., bacitracin, erythromycin)
    - PO antibiotics (e.g., doxycycline, tetracycline, azithromycin)
    - Topical glucocorticoids
    - Topical cyclosporine
  - Demodex infestation
    - Topical tea tree oil x 6 weeks
    - Lotilaner 0.25% opthlalmic solution
    - Oral ivermection

Guidelines

- American Academy of Ophthalmology: Blepharitis Preferred Practice Pattern (2023)
  - Examination of the eye should be performed (physical, slit-lamp biomicroscopy, intraocular pressure)
  - Can do microbiologic testing for patients that have recurrent anterior blepharitis with severe inflammation as well as patients who are not responding to therapy
  - Management
    - Warm compress
    - Artificial tears
    - Eyelid cleansing
    - Eyelid massage to express meibomian glands
    - Topical perfluorohexyloctane
    - ABX (topical or systemic)

Guidelines

- American Academy of Ophthalmology: Blepharitis Preferred Practice
  - Management
    - Antiparasitic medication (metronidazole, ivermectin, lotilaner)
    - Topical anti-inflammatory agents (e.g., corticosteroids, cyclosporine)
    - In-office procedural treatments (e.g., vectored thermal pulsation, microblepharoexfolation)

Lotilaner (Xdemvy)

- Approved by the FDA in July 2023
- Drug Classification
  - Ectoparasiticide
- Indication
  - Treatment of Demodex blepharitis
- Dosing
  - One drop in each eye twice daily (approx. 12 hrs apart) x 6 weeks
- Availability
  - Opthalmic Solution: 0.25%

Gastrointestinal Agents:

Short Bowel Syndrome

Washington State Health Care Authority

Disease State Overview

- Short bowel syndrome (SBS) is a malabsorptive condition often caused by massive resection of the small intestine.
  - Surgical resection for Crohn's disease, malignancy, trauma, radiation, or vascular insufficiency.
- SBS is the most common cause of chronic intestinal failure.
- Affects about 3 out of 1,000,000 people per year.
- Main symptom of SBS is diarrhea. Other signs and symptoms may include bloating, cramping, fatigue, foul-smelling stool, heartburn, vomiting, and weakness.

Disease State Overview

- Management of Acute Phase
  - Characterized by high intestinal fluid losses and metabolic derangements.
  - Starts immediately after resection
  - During initial 3-4 weeks after resection, management goals are to stabilize large fluid and electrolyte losses, and maintain fluid and acid/base balance
    - IV Replacement with NS, K+, and Mg2+
    - Acid Suppression-PPI or H2RA
    - Parenteral Nutrition
    - Enteral feeding

Disease State Overview

- Management in Adaptation Phase
  - Characterized by structural and functional changes to the remaining small bowel and colon in order to increase absorption and slow gastrointestinal transit.
  - Usually lasts one to two years
  - Patients transitioned to oral feedings using stepwise approach over weeks to months
  - Fluid management- goal is to maintain urine output of at least 1L/day
    - ABX for small intestinal overgrowth
    - Ocretotide

Disease State Overview

- Intestinal Failure
  - Reduction in GI function below the minimum necessary for absorption of macronutrients, water, and electrolytes.
  - May be transient or permanent
  - SBS associated failure reverses completely in about 50% of adults within the first two years.
  - GLP-2 analogues for patients unable to be weaned from parenteral nutrition

Guidelines

- American Gastroenterological Association- Management of Short Bowel Syndrome (SBS) (published June 11, 2022) (Best Practice Advice)
  - Initial comprehensive nutritional assessment should be performed by a dietitian experienced in SBS.
    - Long term monitoring should include electrolytes, fluid balance, weight changes, serum micronutrient levels, and bone density
  - Dietary therapy should focus on maintaining compensatory hyperphagia
  - Parenteral nutrition should be initiated and adjusted to meet the patient's fluid, electrolyte, energy, protein, and micronutrient needs
  - Fluids should be given to compensate for all losses and maintain a urine output of at least 1L/day.
    - Glucose-electrolyte oral rehydration solution (ORS)

Guidelines

- American Gastroenterological Association- Management of Short Bowel Syndrome (SBS) (published June 11, 2022)
  - Antimotility and antisecretory agents (PPIs, H2RAs) are frequently necessary to control stool losses.
  - Somatostatin analog (Octreotide)- generally reserved for patients with large volume losses where fluid and electrolyte management is problematic
  - Antidiarrheals help to reduce intestinal motility but also cause a slight reduction in intestinal secretion
    - Loperamide, diphenoxylate with atropine, codeine, and tincture of opium
    - Loperamide is preferred over opiate drugs as it is not addictive.
  - Sustained and delayed release medications should be avoided in patients with SBS. Most PO medications are absorbed within the proximal jejunum and can be used in SBS patients.

Guidelines

- American Gastroenterological Association- Management of Short Bowel Syndrome (SBS) (published June 11, 2022)
  - Glucagon-like-peptide 2 should be employed only after optimizing diet and conventional treatments have been tried in patients with SBS with intestinal failure.

Hematological Agents:

Aminolevulinate Synthase 1-Directed SiRNA

Washington State Health Care Authority

Disease State Overview

- Acute hepatic porphyria (AHP) is a family of rare, genetic diseases characterized by potentially life-threatening attacks with chronic manifestations that negatively impact quality of life and daily functioning.
  - Acute intermittent porphyria (AIP)
  - Hereditary coproporphyria (HCP)
  - Variegate porphyria (VP)
  - ALA dehydratase-deficiency porphyria (ADP)
- Caused by altered activities of enzymes within the heme biosynthetic pathway
- Can cause neurovisceral manifestations (abdominal pain, motor and sensory peripheral neuropathy, neuropsychiatric) or cutaneous photosensitivity (chronic/blistering or acute/non-blistering)

Disease State Overview

- Most common presenting symptom is neuropathic abdominal pain
- Acute intermittent porphyria (AIP) is the most common of the porphyrias
- Management
  - Goal of therapy for an acute attack is to abate the attack as soon as possible and provide symptomatic and supportive treatment until the attack subsides.
  - Prevention of attacks is managed by avoiding exacerbating factors
    - Medications, smoking and alcohol, diet, treatment and prevention of infections, attention to iron stores, suppression of menstrual cycle-related attacks

Guidelines

- American Gastroenterological Association- Clinical Practice Update on Diagnosis and Management of Acute Hepatic Porphyrias: Expert Review (published January 13, 2023) (Best Practice Advice)
  - Women aged 15-50 years with unexplained, recurrent severe abdominal pain without clear etiology should be considered for screening for AHP
  - Management of acute attacked should include pain management, antiemetics, management of systemic arterial hypertension, tachycardia, hyponatremia, and hypomagnesemia if present in addition to intravenous hemin
  - Prophylactic heme therapy or givosiran should be considered in patients with recurrent attacks (four or more per year).

Guidelines

- American Porphyria Foundation- Acute Porphyrias: Emergency Room Recommendations
  - Most effective therapy for an acute attack is Hemin (Panhematin®)
  - Harmful drugs should be stopped immediately and avoided
  - IV glucose loading should be used for mild attacks
  - Hyponatremia, hypomanesemia, and electrolyte imbalances should be corrected and monitored
  - Narcotic analgesics can be used for pain
  - Phenothiazines- nausea, vomiting, or agitation
  - Beta-blockers- control tachycardia and systemic aterial hypertension in patient without hypovolemia
  - Gabapentin, benzodiazepines, and vigabatrin are considered safe to help treat seizures

Givosiran (Givlaari)

- Approved by the FDA in 2019
- Drug Classification
  - Aminolevulinate synthase 1-directed small interfering RNA
- Indication
  - Treatment of adults with acute hepatic porphyria (AHP)
- Dosing
  - 2.5 mg/kg subQ once monthly
- **Warning and Precautions**
  - Risk of acute pancreatitis
- Availability
  - 189 mg/mL single dose vial

Hematological Agents:

Pyruvate Kinase Activators

Washington State Health Care Authority

Disease State Overview

- Pyruvate kinase (PK) deficiency is a rare disorder characterized by the premature destruction of red blood cells, called hemolytic anemia
- Caused by mutations in the PLKR gene leading to a deficiency of the enzyme pyruvate kinase
- Pyruvate kinase helps cells turn glucose into ATP via glycolysis

Disease State Overview

- Management
  - Treatment depends on the age it when the disorder becomes present
    - Before birth- May require intrauterine transfusion
    - Neonatal period- Phototherapy or exchange transfusion
    - Infancy through adulthood- Red blood cell transfusions, folic acid, mitapivat, splenectomy, iron chelation, gene therapy, hematopoietic stem cell transplant
  - Patients should be monitored during routine medical care for symptoms of anemia.
    - Supportive treatments- transfusions, mitapivat, folic acid
    - Splenectomy is for more severe cases
  - Prevention/treatment of iron overload

Hematological Agents:

Other

Washington State Health Care Authority

Disease State Overview

- Peripheral artery disease (PAD) is a common condition where narrowed arteries reduce blood flow to the arms or legs.
  - Usually a sign of atherosclerosis (buildup of fatty deposits in arteries)
- Risk factors
  - Age above 60 years
  - Smoking
  - Hypertension
  - Atherosclerosis
  - Diabetes
  - High cholesterol

Disease State Overview

- Classic symptom of PAD is pain in the legs with physical activity that gets better with rest.
- Other symptoms are pain, aches, cramps with walking (claudication) which can happen in the buttock, hip, thigh, or calf.
- Physical signs of PAD are muscle atrophy, hair loss, skin cool to the touch, decreased/absent pulses in the feet, sores or ulcers in the legs or feet that don’t heal, and cold or numb toes.

Disease State Overview

- Management
  - Overall is aimed at relieving symptoms and lowering the risk of CV disease progression and complications.
    - Preventative therapies include antiplatelet therapy, smoking cessation, lipid-lowering therapy and treatment of diabetes and HTN.
    - Therapeutic lifestyle changes
- Treatments
  - Antithrombotic therapy- aspirin, clopidogrel, ticragelor, vorapaxar
  - Nicotine replacement therapy, varenicline, bupropion
  - Lipid lowering therapy- statins
  - Glycemic control agents
  - Blood pressure control agents

Guidelines

- American College of Cardiology (ACC) and American Heart Association (AHA) (2016)
  - Antiplatelet therapy with aspirin alone (75-325 mg/day) or clopidogrel alone (75 mg/day) is recommended to reduce MI, stroke, and vascular death in patients with symptomatic PAD.
  - In asymptomatic patients with PAD, antiplatelet therapy is reasonable to reduce the risk of MI, stroke or vascular death.
  - Treatment with a statin medication is indicated for all patients with PAD
  - Antihypertensive therapy should be administered to patients with HTN and PAD to reduce risk of MI, stroke, HF, and CV death.
  - The use of ACEIs and ARBs can be effective to reduce the risk of CB ischemic events in patients with PAD

Guidelines

- American College of Cardiology (ACC) and American Heart Association (AHA) (2016)
  - Patients with PAD who smoke cigarettes or other forms of tobacco should be advised at every visit to quit.
  - Patients with PAD who smoke should be assisted in developing a plan for quitting that includes varenicline, bupropion, or nicotine replacement therapy as well as a smoking cessation program.
  - Management of DM in patients with PAD should be coordinated between healthcare teams
  - Cilostazole is an effective therapy to improve symptoms and increase walking distance in patients with claudication
  - Pentoxifylline is not effective for treatment of claudication

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  - Narcotic analgesics can be used for pain
  - Phenothiazines- nausea, vomiting, or agitation
  - Beta-blockers- control tachycardia and systemic arterial hypertension in patient without hypovolemia
  - Gabapentin, benzodiazepines, and vigabatrin are considered safe to help treat seizures

Disease State Overview

- Protein C deficiency is a rare disorder that causes abnormal clotting of blood
- Protein C is a vitamin K dependent anticoagulation protein synthesized in the liver
- Individuals with mild protein C deficiency are at risk of deep vein thrombosis and in severe cases can develop purpura fulminans soon after birth.
  - Type I deficiency (reduced protein C antigen and activity levels)- caused by missense or nonsense mutation
  - Type II deficiency (reduced protein C function with normal antigen levels)- caused by mutations that affect amino acid sequence of protein C

Disease State Overview

- Management
  - Anticoagulation is appropriate for patients with protein C deficiency who develop a thromboembolic event. Management is similar to other individuals with a thromboembolism, with exception of measures to reduce risk of warfarin-induced necrosis.
  - Warfarin-induced skin necrosis management and prevention
    - Acute treatment: discontinue warfarin, administer vitamin K and unfractionated heparin, administer source of protein C (protein C concentrate or fresh frozen plasma)
    - Prevention: low dose warfarin, use of other anticoagulant (dabigatran, rivaroxaban, apixaban, edoxaban)
    - Retreatment: patients can be successfully retreated but protein C concentrate should be used until a stable level of anticoagulation is established

Disease State Overview

- Signs and symptoms of ACS
  - Chest pain
  - Severe dyspnea
  - Diaphoresis
  - Syncope/presyncope and/or palpitations
- Pain may radiate to arms, back, neck, jaw, or epigastric area
- Can occur at rest or precipitated by exercise, stress, extreme weather, etc.
- ACS is a medical emergency

Disease State Overview

- Treatments
  - NSTE-ACS→ can be treated with medications alone or percutaneous coronary intervention (PCI)/stent
  - STEMI → fibrinolytic should be administered if patient cannot get a PCI within 2 hours of first medical contact
- Acute treatment is aimed at providing immediate relief of ischemia and preventing MI expansion and death
  - Morphine
  - Oxygen
  - Nitrates
  - Aspirin
  - Abciximab, eptifibatide, tirofiban
  - LMWH, UFH, bivalirudin
  - Clopidogrel, prasugrel, ticagrelor
  - Beta-blockers
  - ACE Inhibitors

Neuromuscular Agents:

Antimyasthenic/Cholinergic Agents

Washington State Health Care Authority

Disease State Overview

- Myasthenia gravis (MG) is an autoimmune neuromuscular disorder that causes weakness in the muscles.
  - Weakness is due to antibody-mediated immunologic attack directed at protein in the postsynaptic membrane of the neuromuscular junction.
  - Most common disorder of neuromuscular transmission
- Clinical manifestations vary from mild to severe with respiratory failure in others.
- Two clinical forms of MG:
  - Ocular- weakness limited to eyelids and extraocular muscles
  - Generalized- weakness involves variable combination of ocular, bulbar, limb, and respiratory muscles.

Disease State Overview

- Treatments
  - Symptomatic treatment- increase ACh available at the neuromuscular junction
  - Chronic immunotherapies- target underlying immune dysregulation
    - Glucocorticoids and nonsteroidal immunosuppressive and immunomodulatory agents
  - Rapid immunomodulating treatments
  - Surgical treatment (thymectomy)
- Goals of therapy are to help make patients minimally symptomatic or better while minimizing side effects from medications

Disease State Overview

- Lambert-Eaton Myasthenic Syndrome (LEMS)
  - Rare autoimmune disorder of the neuromuscular junction
  - Miscommunication between the nerve cell and the muscles leading to muscle weakness
  - Two different classes:
    - LEMS associated with small cell lung cancer
    - LEMS without cancer
  - Characterized by weakness and fatigue especially of the muscles in the legs and arms
  - Approximately 400 known cases of LEMS in the U.S.
  - LEMS is often misdiagnosed as MG but have key differences:
    - Eye muscle weakness is mild and not the only symptom
    - Severe respiratory muscle weakness is rare
    - Autonomic symptoms that affect LEMS patients are not present in myasthenia gravis
  - Treatment depends on presence of associated cancer.
    - Usually aimed at improving quality of life
    - Symptomatic treatment

Guidelines

- American Academy of Neurology- International Consensus Guidance for Management of Myasthenia Gravis (2020 Update)
  - Ophthalmoparesis or ptosis in ocular MG that does not respond to ACh agents should be treated with immunosuppressant agents
  - Corticosteroids should be used as the initial immunosuppressive agent in ocular MG. Steroid-sparing immunosuppressive agents may be needed when corticosteroids alone are ineffective
  - Rituximab should be considered an early option for patients with muscle specific kinase-Ab+ MG who do not have an adequate response to initial immunotherapy.
  - Eculizumab should be considered in treatment of severe, refractory AChR-positive generalized MG.
  - Eculizumab should be considered after unsuccessful trials of immunotherapies

Amifampridine (Firdapse)

- Approved by the FDA in 2018
- Drug Classification
  - Potassium Channel Blocker
- Indication
  - For the treatment of LEMS in adults and pediatric patients 6 years of age and older
- Dosing
  - 6 years or older, less than 45 kg: 5-15 mg/day PO in 3 or **5 divided doses. Max dose= 50 mg/day**
  - 6 years or older, 45 kg or greater + Adults: 15-30 mg/day PO in 3 or **5 divided doses. Max dose= 100 mg/day**
- Precautions
  - Seizures
- Availability
  - Oral Tablet: 10 mg

Ophthalmic Agents:

Nerve Growth Factors

Washington State Health Care Authority

Disease State Overview

- Neurotrophic Keratitis (NK) is a corneal degenerative disease characterized by a reduction/absence of corneal sensitivity.
- Corneal innervation by the trigeminal nerve is impaired
- Prevalence is less than 50 out of 100,000 people
- Management
  - Promote corneal healing and avoid complications
  - Depends on the disease stage
    - Stage I: Improve quality and transparency of epithelium and to avoid epithelial breakdown.
    - Stage II: Promote persistent epithelial defect healing and prevent development of a corneal ulcer.
    - Stage III: Ulcer healing and prevention of corneal perforation

Guidelines

- Clinical Ophthalmology- Diagnosis and management of neurotrophic keratitis (March 2014)
  - Treatment of NK should be based on disease severity.
  - Use of preservative-free artificial tears may help improve the corneal surface at all stages of disease severity.
  - Steroids may increase the risk of corneal melting and perforation by inhibiting stromal healing and should be used with caution
  - Topical NSAIDs should be avoided
  - In event of stromal melting, topical collagenase inhibitors (N-acetylcysteine) and systemic tetracycline or medroxyprogesterone may be considered.
  - Use of topical ABX eye drops to prevent infection in stages 2 and 3 is recommended.

Vasopressors:

Misc- Oral

Washington State Health Care Authority

Disease State Overview

- Orthostatic hypotension (OH) is a reduction in systolic blood pressure of at least 20 mmHg or a reduction in diastolic blood pressure of at least 10 mmHg.
  - Usually occurs within the first three minutes of standing or head-up tilt on a tilt table
- OH that occurs when the baroreflex is impaired is called neurogenic OH.
- Management
  - Attenuate symptom burden, risk of falls, and reduce target organ damage and mortality
  - Nonpharmacologic measures for asymptomatic patients or mild OH patients
  - Medication is added for patients who do not respond to nonpharmacologic measures

Disease State Overview

- Nonpharmacological measures
  - Removal of offending medications
  - Increase in salt and water intake
  - Lifestyle modification
    - Arise slowly from supine to seated to standing
    - Limit walking in very hot or humid weather, avoid overheating
    - Raise head of the bed 30-45°
  - Dietary interventions
  - Use of compression stockings and abdominal binders

Guidelines

- American Academy of Neurology: Continuum- Management of orthostatic hypotension (2020)
  - Two strategies: expanding intravascular volume and increasing peripheral vascular resistance with other medications
  - Patients with persistent OH symptoms where nonpharmacological measures are insufficient, suggest a regimen that starts with fludrocortisone to augment volume and provide symptom relief
  - Patients with symptoms of OH unresponsive to nonpharmacologic measures such as volume augmentation, suggest short-acting vasoconstrictor agent (midodrine or droxidopa) or atomoxetine.