

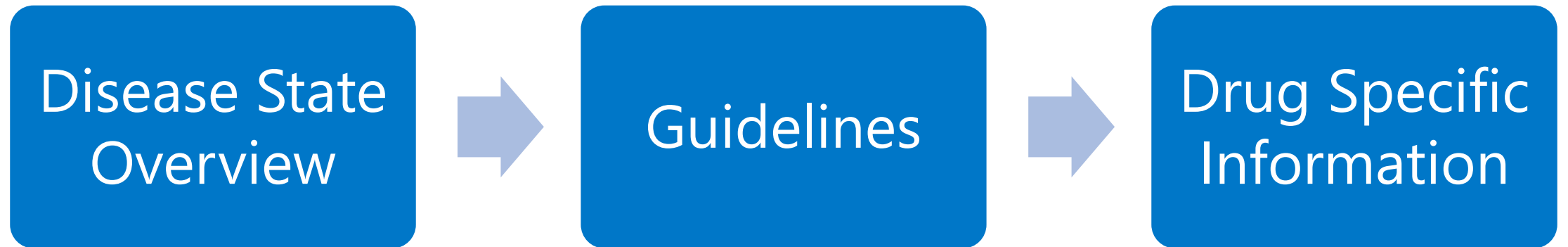
Washington State Drug Utilization Review Board Meeting

April 19, 2023

Marissa Tabile, PharmD

Washington State
Health Care Authority

Clinical Topics



Oncology Agents:

Antiadrenals- Oral

Disease State Overview

- ▶ Adrenocortical carcinomas are rare aggressive tumors that may be functional or nonfunctional.
 - ▶ Forms in the adrenal cortex
 - ▶ Functional tumors secrete hormones
 - ▶ Virilization
 - ▶ Cushing syndrome
 - ▶ Non-functional tumors
 - ▶ Fever, weight loss
 - ▶ Abdominal and back pain
 - ▶ Abdominal fullness
- ▶ Increasing number of adrenocortical carcinomas are identified in asymptomatic patients as incidental findings

Disease State Overview

► Management

- ▶ Complete surgical resection is the only potentially curative treatment.
 - Patients with potentially resectable stage I to III who are surgical candidates, surgical resection is recommended as initial therapy
- ▶ For patients with resected adrenocortical carcinoma, adjuvant therapy is based upon risk of disease recurrence (tumor stage, completeness of resection, and proliferation rate)

Guidelines

- ▶ American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons Medical Guidelines for the Management of Adrenal Incidentalomas (July 2009)
 - ▶ Open adrenalectomy by an experienced surgeon is the procedure of choice.
 - ▶ Patients should undergo en bloc resection of the involved adrenal gland and surrounding tissues. Lymphadenectomy is required as well.
 - ▶ Adjuvant mitotane treatment may be considered post-op in selected patients who have undergone a complete resection of the ACC and have poor prognostic features

Guidelines

- ▶ National Cancer Institute: Childhood adrenocortical carcinoma treatment (PDQ) (2020)
 - ▶ Aggressive surgical approach toward primary tumor and all metastatic sites is recommended if feasible.
 - ▶ Little information available about use of mitotane in children, however response rates appear to be like those seen in adults
 - ▶ Radiation therapy in pediatric patients has not been thoroughly investigated. Adrenocortical tumors are generally considered to be radioresistant.

Guidelines

- ▶ National Cancer Institute: Childhood adrenocortical carcinoma treatment (PDQ) (2019)
 - ▶ Stage I and II
 - ▶ Complete surgical removal is the treatment of choice
 - ▶ Adjuvant mitotane
 - ▶ Stage III
 - ▶ Complete surgical removal with or without regional lymph node dissection
 - ▶ Radiation therapy for patient with localized but unresectable tumors
 - ▶ Chemotherapy with mitotane
 - ▶ Chemotherapy with mitotane + streptozotocin OR mitotane + etoposide + doxorubicin + cisplatin

Guidelines

- ▶ National Comprehensive Cancer Network (NCCN)- Neuroendocrine and Adrenal Tumors (December 2022)
 - ▶ Resectable disease
 - ▶ Open adrenalectomy for suspected carcinoma
 - ▶ Unresectable or suspected metastatic disease
 - ▶ Localized
 - Resect tumor and adjacent lymph nodes
 - If high risk for local recurrence, consider radiation therapy or adjuvant mitotane therapy
 - ▶ Locoregional unresectable or metastatic disease
 - Observation with chest CT
 - Resection of primary tumor and metastases if > 90% removable, particularly if functional
 - Local therapy (radiation, thermal ablative, liver-directed)
 - Systemic therapy

Guidelines

- ▶ National Comprehensive Cancer Network (NCCN)-
Neuroendocrine and Adrenal Tumors (December 2022) --
Principles of Systemic Anti-Tumor Therapy for Locoregional
Unresectable/Metastatic Adrenocortical Carcinoma
 - ▶ Preferred regimens:
 - Cisplatin + etoposide ± doxorubicin ± mitotane
 - Carboplatin + etoposide ± doxorubicin ± mitotane
 - ▶ Other recommended regimens
 - Pembrolizumab ± mitotane
 - Mitotane monotherapy
 - ▶ Useful in certain circumstances
 - Streptozocin ± mitotane

Mitotane (Lysodren)

- ▶ Approved by FDA in 1970
- ▶ Drug Classification
 - ▶ Adrenal cytotoxic agent
- ▶ Indication
 - ▶ Treatment of inoperable, functional or nonfunctional, adrenal cortical carcinoma
- ▶ Dosing
 - ▶ 2g to 6g PO QD in three or four divided doses. Increase dose incrementally to achieve blood concentration of 14-40 mg/L or as tolerated
- ▶ Precautions
 - ▶ Black Box Warning: Adrenal crisis
- ▶ Availability
 - ▶ Tablet: 500 mg

Endocrine and Metabolic Agents:

Hereditary Tyrosinemia Type 1 (HT-1) Agents- Oral

Disease State Overview

- ▶ Hereditary tyrosinemia type 1 (HT1) is a severe disorder of tyrosine metabolism
- ▶ Occurs in 1 in 12,000 to 1 in 100,000 individuals of Northern European descent
- ▶ Caused by deficiency of fumarylacetoacetate hydrolase (FAH)
 - ▶ Fumarylacetoacetate (FAA) is a substrate for FAH, accumulates in FAH-deficient hepatocytes and proximal renal tubular cells causing liver and kidney damage
- ▶ Clinical symptoms typically begin before 2 years old with majority of children presenting before 6 months with evidence of acute liver failure and renal dysfunction.
- ▶ Characterized by severe, progressive liver disease and renal tubular dysfunction.
- ▶ HT1 Management
 - ▶ Nitisinone
 - ▶ Dietary restriction of protein

Guidelines

- ▶ Recommendations in the American College of Medical Genetics and Genomics
 - ▶ Diagnosis and Treatment of tyrosinemia type I: A US and Canadian consensus group review and recommendations
 - ▶ Nitisinone and dietary therapy should be initiated as soon as possible following diagnosis of HT-1. (Evidence quality B)
 - ▶ Nitisinone should be initiated at 1.0 mg/kg/day
 - ▶ Dietary therapy goal is to restrict phenylalanine and tyrosine
 - ▶ Restriction of protein intake is needed

Nitisinone (Orfadin, Nityr)

- ▶ Approved by FDA in 2002
- ▶ Drug Classification
 - ▶ 4-hydroxyphenylpyruvate dioxygenase inhibitor
- ▶ Indication
 - ▶ Treatment of adult and pediatric patients with HF-1 in combination with dietary restriction of tyrosine and phenylalanine
- ▶ Dosing
 - ▶ Adult and Pediatric: 0.5 mg/kg PO BID, increase to 0.75 mg/kg BID. May titrate to max dose of 1 mg/kg BID.
- ▶ Availability
 - ▶ Oral Capsule: 2 mg, 5 mg, 10 mg (generic and Orfadin)
 - ▶ Oral Tablet: 2 mg, 5 mg, 10 mg (Nityr)
 - ▶ Oral Suspension: 4 mg/1 mL (Orfadin)

Neuromuscular Agents:

Antimyasthenic/Cholinergic Agents

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

Pyridostigmine Bromide (Mestinon, Regonol, Mestinon Timespan)

- ▶ First approved by the FDA in 1955 (Mestinon)
- ▶ Mechanism of Action
 - ▶ Cholinesterase inhibitor
- ▶ Indications
 - ▶ Treatment of myasthenia gravis
 - ▶ Reversal of neuromuscular blockade
- ▶ Dosing for MG
 - ▶ 600 mg PO QD, spaced throughout the day. Severe cases may require up to 1500 mg QD.
 - ▶ ER Tablets: 180-540 mg PO QD or BID.
- ▶ Availability
 - ▶ Oral Solution: 60 mg/5 mL (generic, Mestinon)
 - ▶ Tablet: 30mg and 60 mg (generic)
 - ▶ Extended release tablet: 180 mg (generic, Mestinon Timespan)
 - ▶ Injection Solution: 5 mg/1mL (Regonol)

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 4 divided doses. Max dose= 40 mg/day
 - ▶ 6 years or older, 45 kg or greater + Adults: 15-30 mg/day PO in 3 or 4 divided doses. Max dose= 80 mg/day
- ▶ Precautions
 - ▶ Seizures
- ▶ Availability
 - ▶ Oral Tablet: 10 mg

Gastrointestinal Agents:

Short Bowel Syndrome

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.

Teduglutide (Gattex)

- ▶ Approved by the FDA in 2012
- ▶ Drug Classification
 - ▶ Glucagon-like-peptide 2 (GLP-2) analog
- ▶ Indication
 - ▶ Treatment of adults and pediatric patients 1 year of age and older with SBS who are dependents on parenteral support
- ▶ Dosing
 - ▶ Adult and Pediatric: 0.05 mg/kg subQ QD
- ▶ Availability
 - ▶ Kit- Prefilled syringes with diluent, 5 mg vials of Gattex, dosing syringes, alcohol swabs

Hematological Agents- Misc:

Aminolevulinate Synthase 1-Directed SiRNA

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 Porphyrrias: 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 attack should include pain management, antiemetics, management of systemic arterial hypertension, tachycardia, hyponatremia, and hypomagnesemia if present in addition to intravenous heme
 - ▶ 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, hypomagnesemia, 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 arterial 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
- ▶ Availability
 - ▶ 189 mg/mL single dose vial

Ophthalmic Agents:

Nerve Growth Factors

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.

Cenegeermin-bkbj (Oxervate)

- ▶ Approved by FDA in 2018
- ▶ Drug Classification
 - ▶ Recombinant human nerve growth factor
- ▶ Indication
 - ▶ Treatment of neurotrophic keratitis
- ▶ Dosing
 - ▶ One drop in the affected eye(s), six times/day at 2-hour intervals for eight weeks
- ▶ Availability
 - ▶ Multiple dose vial: 0.002% (20 mcg/mL)

Vasopressors:

Misc- Oral

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.

Droxidopa (Northera)

- ▶ Approved by FDA in 2014
- ▶ Drug Classification
 - ▶ Sympathomimetic
- ▶ Indication
 - ▶ For the treatment of orthostatic dizziness, lightheadedness, or the “feeling that you are about to black out” in adult patients with symptomatic neurogenic orthostatic hypotension caused by primary autonomic failure.
- ▶ Dosing
 - ▶ 100 mg PO TID. Titrate by 100 mg TID up to max dose of 600 mg TID
- ▶ Precautions
 - ▶ Black Box Warning: Supine Hypertension
- ▶ Availability
 - ▶ Oral Capsule: 100 mg, 200 mg, 300 mg (generic, Northera)

Midodrine

- ▶ Approved by FDA in 1996
- ▶ Drug Classification
 - ▶ Sympathomimetic
- ▶ Indication
 - ▶ Symptomatic orthostatic hypotension
- ▶ Dosing
 - ▶ 10 mg PO TID
- ▶ Precautions
 - ▶ Bradyarrhythmia
 - ▶ Black Box Warning: Supine hypertension
- ▶ Availability
 - ▶ Oral Tablet: 2.5 mg, 5 mg, 10 mg (generic)

References

- ▶ Adrenocortical carcinoma treatment (PDQ®)–health professional version. Adrenocortical Carcinoma Treatment (PDQ®)–Health Professional Version. https://www.cancer.gov/types/adrenocortical/hp/adrenocortical-treatment-pdq#_38. Accessed April 6, 2023.
- ▶ AGA clinical practice update on management of short bowel syndrome [https://www.cghjournal.org/article/S1542-3565\(22\)00561-4/fulltext](https://www.cghjournal.org/article/S1542-3565(22)00561-4/fulltext). Accessed April 6, 2023.
- ▶ Amfamprifine. Merative Micromedex. Merative. Ann Arbor, MI. Accessed April 6, 2023. <http://www.micromedexsolutions.com>
- ▶ Bunya VY, Woodward MA, Rabiolo A, et al. Neurotrophic keratitis. EyeWiki. https://eyewiki.aao.org/Neurotrophic_Keratitis. Published October 29, 2022. Accessed April 6, 2023.
- ▶ Cenegermine-bkjb. Merative Micromedex. Merative. Ann Arbor, MI. Accessed April 6, 2023. <http://www.micromedexsolutions.com>
- ▶ Childhood adrenocortical carcinoma treatment (PDQ®)–health professional version. Childhood Adrenocortical Carcinoma Treatment (PDQ®)–Health Professional Version. https://www.cancer.gov/types/adrenocortical/hp/child-adrenocortical-treatment-pdq#_820. Accessed April 6, 2023.
- ▶ Chinsky JM, Singh R, Ficicioglu C, et al. Diagnosis and treatment of tyrosinemia type I: A US and Canadian Consensus Group Review and recommendations. *Genetics in medicine : official journal of the American College of Medical Genetics*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5729346/>. Published December 2017. Accessed April 6, 2023.
- ▶ Droxidopa. Merative Micromedex. Merative. Ann Arbor, MI. Accessed April 6, 2023. <http://www.micromedexsolutions.com>
- ▶ Givosiran. Merative Micromedex. Merative. Ann Arbor, MI. Accessed April 6, 2023. <http://www.micromedexsolutions.com>
- ▶ Lambert-Eaton myasthenic syndrome - symptoms, causes, treatment: Nord. Lambert-Eaton Myasthenic Syndrome. <https://rarediseases.org/rare-diseases/lambert-eaton-myasthenic-syndrome/>. Published January 12, 2023. Accessed April 6, 2023.
- ▶ Midodrine. Merative Micromedex. Merative. Ann Arbor, MI. Accessed April 6, 2023. <http://www.micromedexsolutions.com>
- ▶ Mitotane. Merative Micromedex. Merative. Ann Arbor, MI. Accessed April 6, 2023. <http://www.micromedexsolutions.com>

References

- ▶ Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of Myasthenia Gravis. *Neurology*. <https://n.neurology.org/content/96/3/114>. Published January 19, 2021. Accessed April 6, 2023.
- ▶ Neuroendocrine and adrenal tumors, version 2.2021, NCCN clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network : JNCCN*. <https://pubmed.ncbi.nlm.nih.gov/34340212/>. Published December 21, 2022. Accessed April 6, 2023.
- ▶ Nitisinone. Merative Micromedex. Merative. Ann Arbor, MI. Accessed April 6, 2023. <http://www.micromedexsolutions.com>
- ▶ Pimstone NR, Anderon KE, Freilich BL. Acute Porphyrias: Emergency room recommendations. <https://www.porphyrifoundation.org/apf/assets/File/public/professionals/ERGuidelinesAcutePorphyria.pdf>. Accessed April 7, 2023.
- ▶ Pyridostigmine. Merative Micromedex. Merative. Ann Arbor, MI. Accessed April 6, 2023. <http://www.micromedexsolutions.com>
- ▶ Sacchetti, M., Lambiase, A. Diagnosis and management of neurotrophic keratitis. *Clinical Ophthalmology* 2014;8: 571-9.
- ▶ Teduglutide. Merative Micromedex. Merative. Ann Arbor, MI. Accessed April 6, 2023. <http://www.micromedexsolutions.com>
- ▶ Wang B, Bonkovsky HL, Lim JK, Balwani M. AGA Clinical Practice Update on Diagnosis and Management of Acute Hepatic Porphyrias: Expert Review. *Clinical Practice Update*. [https://www.gastrojournal.org/article/S0016-5085\(22\)01356-7/fulltext](https://www.gastrojournal.org/article/S0016-5085(22)01356-7/fulltext). Published January 13, 2023. Accessed April 6, 2023.
- ▶ Zeiger MA, Thompson GB, Duh Q-Y, et al. American Association Of Clinical Endocrinologists And American Association Of Endocrine Surgeons Medical Guidelines For The Management Of Adrenal Incidentalomas. *Endocrine Practice*. <https://www.sciencedirect.com/science/article/pii/S1530891X20428587?via%3Dihub>. Published December 28, 2020. Accessed April 6, 2023.