Washington Pharmacy Advisory Committee Meeting

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Agenda Topics

Prime THERAPEUTICS™

Overview of Disease State

Guidelines

Indications

Dosage & Formulations

Angiotensin Modulators

ANTIHYPERTENSIVES : DIRECT RENIN INHIBITOR COMBINATIONS
ANTIHYPERTENSIVES : DIRECT RENIN INHIBITORS
ANTIHYPERTENSIVES : NEPRILYSIN INHIB (ARNI)-ANGIOTENSIN II RECEPT ANTAG COMBINATIONS

Disease State Description - Angiotensin Modulators

Heart Failure (HF)

- Heart failure (HF) is a common clinical syndrome in which symptoms result from a structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood
- HF may be caused by disease of the myocardium, pericardium, endocardium, heart valves, vessels, or by metabolic disorders
- HF due to left ventricular (LV) dysfunction is categorized according to LV ejection fraction (LVEF)
  - HF with reduced ejection fraction (with LVEF ≤ 40 percent, known as HFrEF; also referred to as systolic HF)
  - HF with preserved ejection fraction (with LVEF ≥ 50 percent, known as HFpEF; also referred to as diastolic HF)
  - HF with mid-range ejection fraction (with LVEF 41 to 49 percent; known as HFmrEF)
- The goals of therapy of HFrEF are to reduce morbidity (i.e., reduce symptoms, improve health-related quality of life and functional status, and decrease the rate of hospitalization), and to reduce mortality

Guidelines - Angiotensin Modulators

The American Heart Association (AHA), American College of Cardiology (ACC), and Heart Failure Society of America (HFSA), 2022

- Published a guideline on the management of heart failure
- For patients at risk for HF (stage A) who have hypertension, the guideline recommends optimal control of blood pressure (BP) using guideline-directed medical therapy (GDMT) (class 1, level A) and a goal BP of < 130/80 mm Hg for patients with a cardiovascular disease (CVD) risk ≥ 10%
- Patients with pre-HF (stage B) and with a left ventricular ejection fraction (LVEF) ≤ 40% should be placed on an ACE inhibitor to prevent symptoms and to reduce mortality (class 1, level A)
  - If a patient is intolerant to an ACE inhibitor and has a history of recent MI, an ARB should be used instead (class 1, level B-R)
- Patients with heart failure with reduced ejection fraction (HFrEF) and New York Heart Association (NYHA) class II to III symptoms are recommended to be placed on the angiotensin receptor/neprilysin inhibitor (ARNI) sacubitril/valsartan (Entresto) to reduce morbidity and mortality (class 1, level A)
  - However, an ACE inhibitor can be prescribed when the use of an ARNI is not feasible (class 1, level A), or an ARB can be used if a patient is intolerant to an ACE inhibitor and if the use of an ARNI is not feasible (class 1, level A)
- GDMT for patients with HFrEF also includes beta blockers (e.g., bisoprolol, carvedilol, metoprolol succinate), mineralocorticoid receptor antagonists (e.g., spironolactone, eplerenone), and sodium-glucose cotransporter-2 inhibitors (SGLT2i)
- Medications used for HFrEF should be optimized to target doses unless not well tolerated
- Dihydropyridine calcium channel blockers (CCBs) may be used for treatment of high BP in patients with HF who do not meet BP goals despite optimization of GDMT

Angiotensin Modulators

Entresto Sprinkle (sacubitril/valsartan)

April 2024 – FDA approved a new oral pellet formulation

- **Entresto Sprinkle contain oral pellets within a capsule and can be substituted in patients unable to swallow tablets**

FDA Indications:

- To reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure. Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal
- For the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older. Entresto reduces NT-proBNP and is expected to improve cardiovascular outcomes

Warnings:

- BBW: Fetal toxicity (when pregnancy is detected, discontinue as soon as possible. Drugs that at directly on the renin-angiotensin system can cause injury and death to the developing fetus.
- CI: History or angioedema related to previous ACE-inhibitors or ARB therapy, concomitant use with ACE-inhibitors, and concomitant use with aliskiren in patients with diabetes

Recommended Dosage:

- Pediatric dosing is based on body weight with a titration regimen (starting dose, second dose, final dose) given twice daily
- Adult starting dosage is 49 mg/51 mg orally twice daily, adjust adult doses every 2 to 4 weeks to the target maintenance dose of 97mg/103mg orally twice daily, as tolerated by the patient

Availability:

- **Film-coated oral pellets within capsules: 6 mg/6 mg; 15 mg/16 mg**

Growth Factors

ENDOCRINE AND METABOLIC AGENTS : INSULIN-LIKE GROWTH FACTORS
ENDOCRINE AND METABOLIC AGENTS : NATRIURETIC PEPTIDES

Disease State Description - Growth Factors

Achondroplasia (ACH)

- Skeletal dysplasia caused by a mutation in the fibroblast growth factor receptor 3 (FGFR3) gene which leads to inhibition of endochondral ossification and impaired bone growth
- Typical clinical features including short stature, limb shortening, and a characteristic facial configuration
- ACH is associated with medical complications including sleep apnea and sleep-disordered breathing, spinal stenosis, kyphosis, recurrent otitis media, and obesity, as well as functional limitations and psychosocial challenges
- Management of ACH focuses upon maximizing functional capacity and monitoring, preventing, and treating complications
- Growth hormone therapy is not recommended and can potentially worsen the disproportionality seen with this population
- Vosoritide is the first FDA approved therapy for ACH

Growth Factors

Voxzogo (vosoritide)

October 2023 – Expanded Indication

- **FDA granted Accelerated Approval to expand indication to increase linear growth in pediatric patients with achondroplasia with open epiphyses to include patients 4.5 months to less than 5 years of age**

FDA Indications:

- Increase linear growth in pediatric patients with achondroplasia with open epiphyses

Warnings:

- Risk of Low Blood Pressure: Transient decreases in blood pressure have been reported; instruct patients to be well-hydrated and have adequate food intake prior to administration

Recommended Dosage:

- Recommended dosage is based on patient's actual body weight
- Administered subcutaneously once daily

Availability:

- For injection: 0.4 mg, 0.56 mg, or 1.2 mg of vosoritide as a lyophilized powder in a single-dose vial for reconstitution

Analgesics, Narcotics - Long
- ANALGESICS : OPIOID AGONISTS - LONG ACTING

Antiemetic/Antivertigo Agents
- ANTIEMETICS / ANTIVERTIGO AGENTS : 5-HT3 RECEPTOR ANTAGONISTS
- ANTIEMETICS / ANTIVERTIGO AGENTS : OTHER
- ANTIEMETICS / ANTIVERTIGO AGENTS : SUBSTANCE P/NEUROKININ 1 (NK1) RECEPTOR ANTAGONISTS
- ANTIEMETICS / ANTIVERTIGO AGENTS : SUBSTANCE P/NEUROKININ 1 RECEPTOR ANTAGONIST COMBINATIONS

Hepatitis C Agents
- ANTIVIRALS : HEPATITIS C AGENTS - DIRECT ACTING ANTIVIRALS
- ANTIVIRALS : HEPATITIS C AGENTS - MISC

Contraceptives, Other
- CONTRACEPTIVES : NON-HORMONAL - VAGINAL

Androgenic Agents
- ENDOCRINE AND METABOLIC AGENTS : ANDROGENS - TESTOSTERONE

Hyperparathyroid Agents
- ENDOCRINE AND METABOLIC AGENTS : CALCIMIMETIC AGENTS – ORAL

Nutritionals, Caloric Agents
- ENDOCRINE AND METABOLIC AGENTS : HOMOCYSTINURIA AGENTS – ORAL

Urea Cycle Disorders
- ENDOCRINE AND METABOLIC AGENTS : HYPERAMMONEMIA AGENTS – ORAL

Diuretics
- ENDOCRINE AND METABOLIC AGENTS : MINERALOCORTICOID RECEPTOR ANTAGONISTS

Uterine Disorder Treatments
- ENDOCRINE AND METABOLIC AGENTS : PITUITARY SUPPRESSANT COMBINATIONS

Antibiotics, GI
- GASTROINTESTINAL AGENTS : LIVE FECAL MICROBIOTA

Immunosuppresive, Oral
- IMMUNOSUPPRESSIVE AGENTS : ROCK INHIBITORS

Antimigraine Agents, Others
- MIGRAINE AGENTS : CALCITONIN GENE-RELATED PEPTIDE (CGRP) RECEPTOR ANTAGONISTS

Antimigraine Agents, Triptans
- MIGRAINE AGENTS : SELECTIVE SEROTONIN AGONISTS 5-HT(1)

Ophthalmics, Vasoconstrictor
- OPHTHALMIC AGENTS : ALPHA ADRENERGIC AGONISTS

PAH Agents, Oral and Inhaled
- PULMONARY HYPERTENSION AGENTS : ENDOTHELIN RECEPTOR ANTAGONISTS
- PULMONARY HYPERTENSION AGENTS : PHOSPHODIESTERASE INHIBITORS (PDEI)
- PULMONARY HYPERTENSION AGENTS : PROSTACYCLIN RECEPTOR AGONISTS
- PULMONARY HYPERTENSION AGENTS : PROSTAGLANDIN VASODILATORS
- PULMONARY HYPERTENSION AGENTS : SGC STIMULATOR

Androgenic Agents

ENDOCRINE AND METABOLIC AGENTS : ANDROGENS - TESTOSTERONE

Androgenic Agents

Discontinuation

- December 2023 - Fortesta (testosterone)
  - Endo discontinued Fortesta (testosterone gel metered 10 mg/0.5 g)
  - Generics remains

- September 2024 - Depo-testosterone (testosterone cypionate)
  - FDA announced that Pfizer will discontinue marketing Depo-testosterone injections
  - Generics remains

PAH Agents, Oral and Inhaled

PULMONARY HYPERTENSION AGENTS : ENDOTHELIN RECEPTOR ANTAGONISTS
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PULMONARY HYPERTENSION AGENTS : SGC STIMULATOR

PAH Agents, Oral and Inhaled

Discontinuation

- **May 2024 – Ventavis (iloprost)**
  - **Actelion/Philips Respironics has announced discontinuation of the I-neb AAD system as well as associated supplies (e.g., medication discs used for administering the solution)**
  - **Iloprost (Ventavis) solution in the strengths of 10 ug/mL and 20 ug/mL is also being discontinued**