Wyoming Drug Utilization Review

Pulmonary Hypertension

Written by Suyasha Pradhanang PharmD, 2024

Pulmonary hypertension (PH) is a progressive disease that is characterized by elevated pulmonary artery pressure, which can lead to hypertrophy and remodeling of the right ventricle of the heart.[1] Due to the complexity of PH, treatment generally focuses on the underlying conditions and requires a multifaceted approach.[2] It is a rare condition and is estimated to affect about 15-50 people per million within the US and Europe.[3] There are 5 distinct groups of PH.

Group 1 PH is due to pulmonary arterial hypertension. Treatment of patients who are diagnosed with group 1 PH can be very complex. Treatment strategies are dependent on an initial vasodilator challenge through the vasoreactivity test.[2] The agent used in this vasodilator challenge can vary, however, the typical agent used is either nitric oxide or inhaled iloprost. Epoprostenol can also be used, however is less feasible compared to the first two agents. If patients respond to the vasodilator challenge, then long-term vasodilator therapy is the mainstay.[2] The most common long-term treatment is high-dose calcium channel blockers (CCBs). Agents that are predominantly used are amlodipine, felodipine, nifedipine, and diltiazem[5]. Amlodipine and felodipine are increasing in popularity due to their longer half-life and better tolerability[2]. The guidelines do not recommend one agent over the other, and due to the lack of data, the choice of agent is up to the disciplinary team. Patients who did not undergo a vasoreactivity test or were nonresponders should not be started on CCBs.[2]

Another class of medication for the treatment of group 1 PH is endothelin receptor antagonists (ERAs). These work by inhibiting the endothelin receptors within the endothelial cells and promoting vasodilation and reduction in pulmonary vascular resistance.[7] The third class of agents is phosphodiesterase 5 (PDE-5) inhibitors. This class of medications inhibits the breakdown of cyclic guanosine monophosphate (cGMP) promoting vasodilation of the smooth muscles.[7] The two approved agents include sildenafil and tadalafil. Patients in group 1 who are at a lower risk of developing PH are generally started with these agents.[5] Multiple studies have shown that PDE-5 inhibitors improve exercise capacity (6-minute walk test), symptoms, and cardiopulmonary hemodynamics in patients.[5]Soluble guanylate cyclase (sGC) stimulators are another class that is approved for treatment in this group. These work by stimulating sGC which increases the cGMP levels, leading to the vasodilation of smooth muscles.[9] The only agent in this class is riociguat.

Finally, prostacyclin analogs and prostacyclin receptor agonists may be used. The prostacyclin analogs mimic the effects of prostacyclin, promote vasodilation, and inhibit platelet aggregation.[7] The three agents within this class are epoprostenol, iloprost, and treprostinil. Epoprostenol is administered IV and is generally administered as inpatient due to its short half-life and the need for continuous infusions.[7] Iloprost is administered by inhalation whereas, treprostinil is available for subcutaneous, IV, inhaled, and oral use due to its greater stability.[2,7]

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There is no data supporting one agent over another. Due to the relatively shorter half-lives of the prostacyclin analogues, a prostacyclin receptor agonist was developed. Selexipag works similarly to prostacyclin analogs and has been shown to decrease the risk of hospitalization, death, long-term oxygen use, and lung transplantation.[7]

While there are many treatment classes available for patients in group 1, the guidelines do not recommend any first-line vs second-line agents for the management of PH in this group. This decision depends on the patient's condition and provider preference.

Drug agent	Dosing[6]	Adverse effects[2]
Calcium Channel Blockers (CCB)[2,6]		
Amlodipine	Adults: 2.5 mg per day. Gradually increased to maximally tolerated dose over days to weeks	Hypotension and edema
Nifedipine	Adults: 30 mg per day. Gradually increased to maximally tolerated dose over days to weeks	Hypotension and edema
Diltiazem ER	Adults: 120 mg per day. Gradually increased to maximally tolerated dose over days to weeks	Hypotension and edema
Endothelin Receptor Antagonists (ERAs)[2]		
Ambrisentan	Adults: 5 mg and 10 mg	Increased peripheral edema, teratogenic
Bosentan	Adults: 125 mg BID	Increase in liver transaminases, reduces efficacy of oral contraceptives teratogenic
Macitentan	Adults: 10 mg	Reduces hemoglobin to ≤8 g/d, teratogenic
Phosphodiesterase 5 (PDE-5) Inhibitors[2,5]		
Sildenafil	Adults: 20 mg TID	Headache, flushing
Tadalafil	Adults: 40 mg QD	Headache, flushing
Soluble Guanylate Cyclase (sGC) stimulator[2]		
Riociguat	Adults: 2.5 mg TID	Headache, flushing
Prostacyclin Analogs[2,8]		
Epoprostenol	Adults: 5 mg and 10 mg	Pump malfunction is possible, injection site reactions
Iloprost	Adults: 2.5 mcg/dose, increased to 5 mcg/dose if tolerated, 6-9 times a day[8]	Cough, flushing, headache, nausea, hypotension[8]
Treprostinil	Adults: 10 mg	Infusion-site pain and swelling
Prostacyclin Receptor Agonists[2]		
Selexipag	Adults: 2.5 mg TID	Headache, diarrhea, jaw pain, nausea

Group 2 PH is primarily seen in patients with left heart disease (LHD). It includes conditions such as heart failure with reduced, mildly reduced, or preserved ejection fraction, left-sided valvular heart disease, and other cardiovascular conditions that lead to PH.[2]Treating patients' underlying cardiac conditions primarily consists of monotherapy or combination therapy with loop diuretics, thiazide diuretics, and mineralocorticoid receptor antagonists for the management of fluid retention, along with an individualized approach in addressing the cardiac issues.[2]

Group 3 PH is associated with lung diseases. Among these, chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD) are more predominant underlying conditions.[9] Due to the multifactorial nature of PH, treatment should focus on treating the underlying pulmonary conditions. This includes supplemental oxygen for hypoxia, enrolling patients in pulmonary rehabilitation programs, and referring them to PH centers.[2] Limited data have shown some improvement with PDE-5 inhibitors in this group.[2,9] Due to the lack of robust studies, the guidelines currently do not recommend PDE-5 inhibitors in this patient group and recommend that these patients get referred to PH centers for individualized treatments.[2]

Group 4 PH is due to the chronic thromboembolic obstruction of the pulmonary arteries (CTEPH). The recommended treatment for CTEPH patients is lifelong anticoagulation therapy. While the guidelines do not have a specific agent they recommend, they do mention that vitamin K antagonists (VKAs) like warfarin are recommended by experts for the background therapy for patients with CTEPH.[2] Yang et al.[10] recommend patients go through a multidisciplinary evaluation to determine an individualized treatment approach.

Group 5 PH is due to unclear and/or multifactorial mechanisms, thus cases of PH without a clear mechanism or a clear understanding of the underlying condition are within this group. Some of the conditions within group 5 PH include: hematologic disorders, sarcoidosis, thyroid disease, renal failure, fibrosing mediastinitis, etc.[2,11] Group 5 PH includes conditions that are least understood. While the guidelines do not recommend a specific treatment, its management lies vastly on treating the underlying conditions.

References

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The P&T Committee met for its quarterly business meeting on August 14, 2025.

Highlights of this meeting include:

This is Garry Needham's last meeting after serving a full twelve years on the Committee. We are looking for a pharmacist to fill this position. Interested pharmacists can submit a CV to Aimee Lewis at alewis13@uwyo.edu.

Dr. Paul Johnson has returned to full time clinical practice. Dr. Tracey Haas has filled his position as the Medical Director.

Elevidys will be limited to ambulatory patients.

The maximum dose of Belbuca has been increased to 1800 mcg per day to match the product label.

Continuous glucose monitors will be allowed for pregnant women with type 1 diabetes, with or without the use of insulin.

The Committee voted to treat alopecia areata and vitiligo as medical conditions instead of cosmetic. JAK inhibitors for alopecia areata will require a trial and failure of a high potency corticosteroid for at least 90 days and a SALT score greater than 20%. In addition, consultation with a dermatologist will be required. Leqselvi, Olumiant and Litfulo were referred to the Department of Health for cost analysis and PDL placement. Opzelura for vitiligo will require a trial and failure of a medium or high potency corticosteroid for 90 days prior to approval.

Vanrafia, Yutrepia, Andembry, Qfitlia, Briumvi and Enflonsia were limited to indication and referred to the Department of Health for cost analysis and PDL placement.

Vykat was limited to indication.

All prior authorization criteria are open for public comment. Comments should be sent by email to alewis13@uwyo.eduby September 15, 2025.

The next P&T Committee meeting will be held November 13, 2025 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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