# Overview

## Table 1: Formulary Pulmonary Hypertension Agents:

<table>
<thead>
<tr>
<th>Class</th>
<th>Generic (Brand)</th>
<th>Strengths:</th>
<th>Form</th>
<th>Restriction Notes:</th>
<th>Cost/ Month:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Channel Blockers (CCB)</td>
<td>Amlodipine</td>
<td>2.5mg, 5mg, 10mg</td>
<td>QL</td>
<td>Restricted to 1 tablet per day. Submit PA for larger quantities.</td>
<td>$4.24</td>
</tr>
<tr>
<td></td>
<td>Nifedipine</td>
<td>IR: 10mg, 20mg</td>
<td></td>
<td></td>
<td>$45.79</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ER: 30mg, 60mg, 90mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CR: 30mg, 60mg, 90mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>XL: 30mg, 60mg, 90mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diltiazem</td>
<td>IR: 30mg, 60mg, 90mg, 120mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LA: 120mg, 180mg, 240mg, 300mg, 360mg, 420mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ER: 60mg, 90mg, 120mg, 180mg, 240mg, 300mg, 360mg, 420mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD: 60mg, 120mg, 180mg, 240mg, 300mg, 360mg, 420mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>XT: 120mg, 180mg, 240mg, 300mg, 360mg, 420mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phosphodiesterase-5 Inhibitors (PDE-5i)</td>
<td>Sildenafil (Revatio)</td>
<td>20mg</td>
<td>PA</td>
<td>PAH Class II-IV with IPAH with (-) vasoreactivity test or (+) vasoreactivity test and use of CCB</td>
<td>$111.29</td>
</tr>
<tr>
<td></td>
<td>Tadalafil (Adcirca)</td>
<td>10mg</td>
<td>PA</td>
<td>Inadequate response to adequate trial of Sildenafil.</td>
<td>$2795.93</td>
</tr>
<tr>
<td>Endothelin Receptor Antagonists (ERA)</td>
<td>Bosentan (Tracleer)</td>
<td>62.5mg, 125mg</td>
<td>PA</td>
<td>PAH Class II: Adequate trial of PDE-5 inhibitor is required. PAH Class III-IV: IPAH with (-) vasoreactivity test or (+) vasoreactivity test and use of CCB</td>
<td>$9241.41</td>
</tr>
<tr>
<td></td>
<td>Ambrisentan (Letairis)</td>
<td>5mg, 10mg</td>
<td>PA</td>
<td></td>
<td>$8082.33</td>
</tr>
<tr>
<td></td>
<td>Macitentan (Opsumit)</td>
<td>10mg</td>
<td>PA</td>
<td></td>
<td>$7555.60</td>
</tr>
<tr>
<td>Prostanoids</td>
<td>Epoprostenol (Flolan, Veletri)</td>
<td>Glycine (Flolan), Arginine (Veletri) : 0.5mg Solution, 1.5mg Solution</td>
<td>PA</td>
<td>PAH Class IV IPAH with (-) vasoreactivity test or (+) vasoreactivity test and use of CCB</td>
<td>$2730.06</td>
</tr>
<tr>
<td></td>
<td>Iloprost</td>
<td>Ventavis 20mcg/mL Nebulization.</td>
<td>PA</td>
<td></td>
<td>$13,080</td>
</tr>
<tr>
<td></td>
<td>Tromethamine Inhalation</td>
<td></td>
<td></td>
<td></td>
<td>$13,149</td>
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<tr>
<td></td>
<td>Treprostinil IV or SQ</td>
<td>1 mg/mL, 2.5 mg/mL, 5 mg/mL, 10 mg/mL</td>
<td>PA</td>
<td></td>
<td>$14,030.74</td>
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<tr>
<td></td>
<td>(Remodulin)</td>
<td>Treprostinil Inhalation (Tyvaso)</td>
<td>1.74mg/2.9mL Solution, Starter kit also available (includes nebulizer).</td>
<td>PA</td>
<td>PAH Class III with (-) vasoreactivity test or (+) vasoreactivity test and use of CCB as step therapy to adequate use of PDE-5 inhibitors and/or ERA.</td>
</tr>
</tbody>
</table>
Treprostinil PO (Orenitram)  
0.125mg, 0.25, 1mg, 2.5mg  
PA  
Restricted to PAH Class II with treatment failure of Sildenafil, Tadalafil, Bosentan, Macitentan, and Ambrisentan. Not for use as combination therapy.  
$8424

Soluble Guanyl Cyclase (sGC) Stimulants  
Riociguat (Adempas)  
0.5mg, 1mg, 1.5mg, 2mg, 2.5mg  
PA  
CTEPH Class II or higher with inoperable or recurrent disease OR PAH Class II or higher with treatment failure of Sildenafil and Tadalafil.  
$8156

IP Receptor Agonists  
Selexipag (Uptravi)  
200mcg, 400mcg, 800mcg, 1000mcg, 1200mg, 1400mcg, 1600mcg  
PA  
Restricted to patients with PAH Class III with (−) vasoreactivity test or (+) vasoreactivity test and use of CCB (if appropriate) and inadequate response to dose optimized use of PDE-5 inhibitors and ERA.  
$18,121

Verification that members are NOT abusing methamphetamine is required for initial and subsequent requests. Costs based on utilization data unless specified elsewhere.

**Clinical Justification:**

Pulmonary Hypertension drugs are restricted based on clinical evidence available. Calcium channel blockers are the preferred agent in patients who can tolerate them, and who have shown good response during right heart catheterization. Drugs are restricted based on WHO Functional Class. ERAs are not benign drugs. They can potentially cause LFT elevations in patients who take them chronically. Sildenafil is widely available and relatively benign, thus carries few restrictions, while intravenous prostanoids carry significant risk, and should not be used unless all other therapeutic agents have been exhausted.

**Triage:**

- **Appropriate diagnosis:** WHO Group, and WHO Functional Class (if available)
- **Provider Specialty**
- **Current Pulmonary Hypertension drugs**
- **Toxicology Screen Results**

**EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION**

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HSPJ Medical Review Guidelines (UM06).

**Calcium Channel Blocker**

**Nifedipine, Amlodipine**

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A

**Diltiazem (All Formulations)**

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
**Phosphodiesterase-5 Inhibitors (PDE-5i)**

**Sildenafil (Revatio)**
- **Coverage Criteria:** Reserved for patients with IPAH with a (-) vasoreactivity test or (+) vasoreactivity test and use of/contraindication to Calcium Channel Blocker use. Members must have WHO Functional Class II-IV disease.
- **Limits:** None
- **Required Information for Approval:** Results of member’s right heart catheterization/vasoreactivity test, Chart notes documenting WHO Functional Class II or higher disease. Prescription must be written by a cardiologist, pulmonologist, or critical care provider.

**Tadalafil (Adcirca)**
- **Coverage Criteria:** Step therapy to inadequate response/treatment failure on sildenafil. Patient’s must have IPAH with a (-) vasoreactivity test or (+) vasoreactivity test and use of/contraindication to Calcium Channel Blocker use. Members must have WHO Functional Class II-IV disease.
- **Limits:** None
- **Required Information for Approval:** Documentation of an adequate trial of sildenafil. Results of member’s right heart catheterization/vasoreactivity test, Chart notes documenting WHO Functional Class II or higher disease. Prescription must be written by a cardiologist, pulmonologist, or critical care provider.

**Endothelin Receptor Antagonists (ERAs)**

**Bosentan (Tracleer), Macitentan (Opsumit), Ambrisentan (Letairis)**
- **Coverage Criteria:** PAH Class II: Adequate trial of PDE-5 inhibitor is required. PAH Class III-IV: IPAH with (-) vasoreactivity test or (+) vasoreactivity test and use of/contraindication to Calcium Channel Blocker use. Must be prescribed by a cardiologist or pulmonologist.
- **Limits:** None
- **Required Information for Approval:** Chart notes documenting patients WHO Functional Class. Fill history of PDE-5 inhibitors. IPAH with a (-) vasoreactivity test or (+) vasoreactivity test and use of/contraindication to Calcium Channel Blocker use.

**Prostanoids**

**Epoprostenol (Flolan, Veletri), Iloprost (Ventavis), Treprostinil IV/SQ (Remodulin)**
- **Coverage Criteria:** PAH Functional Class IV with a (-) vasoreactivity test or (+) vasoreactivity test and use of/contraindication to Calcium Channel Blocker use.
- **Limits:** None
- **Required Information for Approval:** Chart notes documenting WHO Functional Class. Fill history of calcium channel blockers.

**Treprostinil (Tyvaso)**
- **Coverage Criteria:** PAH Functional Class III or higher. Step therapy to use of PDE-5 inhibitors and/or ERA, with a (-) vasoreactivity test or (+) vasoreactivity test and use of/contraindication to Calcium Channel Blocker use.
- **Limits:** None
- **Required Information for Approval:** Chart notes documenting WHO Functional Class. Fill history of calcium channel blockers, PDE-5 inhibitors, and ERA (if applicable.)

**Treprostinil Diethanolamine (Orenitram)**
- **Coverage Criteria:** Restricted to members with WHO Group 1 (PAH) with a (-) vasoreactivity test or (+) vasoreactivity test and use of/contraindication to Calcium Channel Blocker use. WHO Functional Class II-IV disease, as step therapy to treatment failure of sildenafil, tadalafil, bosentan, macitentan, and ambrisentan. Must be prescribed by a cardiologist, pulmonologist, or critical care specialist. For use as monotherapy only.
- **Limits:** None
- **Required Information for Approval:** Right heart catheterization with vasoreactivity results. Documentation of member’s WHO functional class. Fill history of sildenafil, tadalafil, bosentan, macitentan, and ambrisentan. To be used ONLY as monotherapy.
Soluble Guanylate Cyclase Stimulants

**Riociguat (Adempas):**
- **Coverage Criteria:** WHO Group IV disease with Functional class II or higher disease that is inoperable or recurrent OR Group I PAH as step therapy to treatment failure of Sildenafil and Tadalafil with a (-) vasoreactivity test or (+) vasoreactivity test and use of/contraindication to Calcium Channel Blocker use. Must be prescribed by a cardiologist or pulmonologist.
- **Limits:** None
- **Required Information for Approval:** Chart notes documenting WHO Functional Class and WHO Group. Documentation of the member’s right heart catheterization, fill history of calcium channel blockers (if applicable).

**IP Receptor Agonist**

**Selexipag (Uptravi):**
- **Coverage Criteria:** Restricted to patients with PAH Class III with (-) vasoreactivity test or (+) vasoreactivity test and use of CCB (if appropriate) and inadequate response to dose optimized use of PDE-5 inhibitors and ERA.
- **Limits:** None
- **Required Information for Approval:** Chart notes documenting WHO Functional Class and WHO Group. Documentation of the member’s right heart catheterization, fill history of calcium channel blockers (if applicable), compliant use of Sildenafil or Tadalafil, and Macitentan, Bosentan, or Ambrisentan.

## REFERENCES

1. HPSJ Formulary Criteria

## REVIEW & EDIT HISTORY

<table>
<thead>
<tr>
<th>Document Changes</th>
<th>Reference</th>
<th>Date</th>
<th>P&amp;T Chairman</th>
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<tr>
<td>Creation of Policy</td>
<td>PAH Class Review 5-21-2013.docx</td>
<td>5/2013</td>
<td>Jonathan Szkotak, PharmD BCACP</td>
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<tr>
<td>Update Policy</td>
<td>Drug Class Review – Respiratory disorders – Pulmonary Hypertension 2015-11.docx</td>
<td>11/2015</td>
<td>Johnathan Yeh, PharmD</td>
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<tr>
<td>Update Policy</td>
<td>HPSJ Coverage Policy – Respiratory disorders – Pulmonary Hypertension 2016-11.docx</td>
<td>12/2016</td>
<td>Johnathan Yeh, PharmD</td>
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</tbody>
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*Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy*