Pulmonary Arterial Hypertension (PAH) Agents:
Revatio™ (sildenafil), Ventavis® (iloprost), Tracleer®
(bosentan), Letairis™ (ambrisentan), Adcirca®
(tadalafil), Tyvaso® (treprostinil), Remodulin®
(treprostinil), Flolan®/Veletri® (epoprostenol),
Adempas® (riociguat), Opsumit® (macitentan),
Orenitram® (treprostinil), Uptravi® (selexipag), Alyq
(tadalafil)

I. Medication Description

Pulmonary Arterial Hypertension (PAH) is a condition characterized by unusually high and persistent pulmonary
artery pressure. Common symptoms patients initially experience are shortness of breath, fatigue, and fainting. As the
disease progresses, symptoms become more acute and patients may develop cyanosis, edema, and
angina. The disease is progressive and can lead to right-sided heart failure and death. Several biological drug
targets have been identified as mechanisms involved in PAH. Phosphodiesterase-5 inhibitors inhibit a specific
phosphodiesterase enzyme found in the smooth muscle of the pulmonary vasculature, thus resulting in a
relaxation of pulmonary smooth muscles and ultimately, a decrease in resistance. Prostacyclin analogs decrease
pulmonary vascular resistance by taking advantage of the vasodilatory effects of this prostaglandin. Endothelial-
receptor antagonists block endothelin’s ability to bind to receptors on lung blood vessels, thus preventing
constriction of these vessels. Soluble guanylate cyclase stimulators decrease vascular tone independent of nitric
oxide.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every
request.

All medications in this policy may be covered under the pharmacy benefit if they are self-administered. Flolan,
Veletri, Remodulin, Ventavis may also be covered under the medical benefit if they are administered by a
healthcare professional.

III. Policy

Coverage of the pulmonary arterial hypertension agents in this policy is provided in accord with the following:

- For Pulmonary Arterial Hypertension (all agents in this policy):
  - Patient is followed by a cardiologist or pulmonologist AND
  - Patient has been evaluated with a right heart catheterization AND
Patient is diagnosed with pulmonary arterial hypertension (WHO Group 1) based on the following:

- Mean pulmonary arterial pressure (mPAP) greater than or equal to 25mm Hg AND
- Pulmonary capillary wedge pressure (PCWP) or pulmonary artery occlusion pressure (PAOP) less than or equal to 15mm Hg AND
- Pulmonary vascular resistance (PVR) greater than 3 Wood units AND

- For Chronic Thromboembolic Pulmonary Hypertension (Adempas only):
  - Patient is followed by a cardiologist or pulmonologist AND
  - Patient has been evaluated with a ventilation-perfusion (VQ) scan AND
  - After surgical treatment or inoperable AND
  - Patient is diagnosed with chronic thromboembolic pulmonary hypertension with the following signs/symptoms:
    - Chest discomfort/angina, fatigue, lightheadedness, or syncope AND
    - Pulmonary flow murmur or bruit OR
    - History of recurrent pulmonary emboli

IV. Quantity Limitations

- Revatio: 90 tablets per 30 days
- Revatio Oral Suspension: 224 mL (2 bottles) per 30 days
- Adcirca: 60 tablets per 30 days
- Alyq: 60 tablets per 30 days
- Flolan: Individualized per patient.
- Veletri: Individualized per patient.
- Remodulin: Individualized per patient.
- Tyvaso®: 1 box of 28 ampules per 28 days.
- Ventavis: 270 ampules per 30 days.
- Letairis: 30 tablets per 30 days.
- Tracleer:
  - 62.5mg: 60 tablets per 30 days
  - 125mg: 60 tablets per 30 days
  - 32 mg tablets for oral suspension: 120 tablets per 30 days
- Adempas: 90 tablets per 30 days
- Opsumit: 30 tablets per 30 days
- Orenitram: Individualized per patient.
- Uptravi
  - Titration (first two months): up to 140 x 200mcg tabs per month and one titration pack
  - Maintenance: (each individual strength): 60 tablets per 30 days

V. Coverage Duration

Coverage will be granted indefinitely through the life of this policy once the initial criteria are met.
VI. Coverage Renewal Criteria  
n/a  

VII. Billing/Coding Information  

- Pertinent indications: I27.0, I27.2  
- Revatio:  
  - J3490  
  - 10 mg/12.5 mL solution for injection  
  - 20 mg tablets  
  - 10 mg/ml oral suspension  
  - Medical benefit when administered by a healthcare professional  
  - Pharmacy benefit  
- Flolan:  
  - J1325 (each billable unit = 0.5 mg)  
  - 0.5mg, 1.5mg powder for injection  
  - Medical benefit when administered by a healthcare professional  
  - Pharmacy benefit when self-administered  
- Veletri:  
  - J1325 (each billable unit = 0.5mg)  
  - 0.5mg, 1.5mg powder for injection  
  - Medical benefit when administered by a healthcare professional  
  - Pharmacy benefit when self-administered  
- Remodulin:  
  - J3285 (each billable unit = 1 mg)  
  - 1mg/ml, 2.5mg/ml, 5mg/ml, and 10mg/ml vials for continuous SC infusion  
  - Medical benefit when administered by a healthcare professional  
  - Pharmacy benefit when self-administered  
- Ventavis:  
  - Q4074 (each billable unit = up to 20mcg)  
  - 10mcg/ml or 20mcg/ml ampules (1 ml each)  
  - Medical benefit when administered by a healthcare professional  
  - Pharmacy benefit when self-administered  
- Tyvaso:  
  - 0.6mg/ml and 1.74 mg/2.9 mL ampules for inhalation  
  - Pharmacy benefit  
- Tracleer:  
  - 62.5mg, 125mg oral tablets  
  - 32 mg tablets for oral suspension  
  - Pharmacy benefit  
- Letairis:  
  - 5mg, 10mg oral tablets  
  - Pharmacy benefit
- **Adcirca:**
  - 20mg oral tablets
  - Pharmacy benefit

- **Adempas:**
  - 0.5mg, 1mg, 1.5mg, 2mg, 2.5mg oral tablets
  - Pharmacy benefit

- **Alyq**
  - 20 mg oral tablets
  - Pharmacy benefit

- **Opsumit®:**
  - 10mg oral tablets
  - Pharmacy benefit

- **Orenitram®**
  - 0.125mg, 0.25mg, 1mg, 2.5mg, 5mg oral tablets
  - Pharmacy benefit

- **Uptravi®**
  - 200mcg, 400mcg, 600mcg, 800mcg, 1000mcg, 1200mcg, 1400mcg, and 1600mcg oral tablets; Titration pack
  - Pharmacy benefit

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**VIII. Summary of Policy Changes**

- **1/1/12:**
  - Addition of Veletri to policy
  - Removal of Black Box Warning from Letairis
  - Implement PA reviews of Ventavis, Flolan, and Veletri

- **9/15/12:** Longer approval duration applies

- **12/15/12:**
  - Requirement of hemodynamic diagnostic testing results and right heart catheterization added for initial coverage
  - Warnings edited (reference to full prescribing information made)
  - Coverage of Revatio limited to patients who are at least 18 years of age

- **12/15/13:**
  - Flolan/Veletri pharmacy coverage provided
  - Adempas and Opsumit added to policy

- **3/31/14:** restriction of Revatio to patients aged 18 and older removed

- **6/15/14:** Orenitram added to policy

- **1/1/15:** Veletri 0.5mg added to policy

- **7/1/15:** formulary distinctions made

- **3/15/16:** addressed Tracleer 125mg quantity limits of 60/month; Uptravi added to policy text

- **11/15/16:** updated quantity limits for Orenitram to allow for appropriate titration dosing

- **1/1/17:** no policy changes
IX. References

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17. Tyvaso® package insert, revised 10/2017
18. Ventavis® package insert, revised 10/2017
19. Tracleer® package insert, revised 5/2019
20. Letairis™ package insert, revised 8/2019
<table>
<thead>
<tr>
<th>Reference</th>
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<tbody>
<tr>
<td>21. Veletri® package insert, revised 12/2018</td>
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<tr>
<td>23. Adempas® package insert, revised 1/2018</td>
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<td>24. Opsumit® package insert, revised 4/2019</td>
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<tr>
<td>26. Orenitram® package insert, revised 10/2019</td>
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<td>27. Uptravi® package insert, revised 9/2019</td>
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*These guidelines are not applicable to benefits covered under Medicare Advantage. Medicare Advantage benefit coverage requests are reviewed in accordance with the guidance set forth in Chapter 15 Section 50 of the Centers for Medicare & Medicaid Services Medicare Benefit Policy Manual.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.