Treatment Guidelines for Pulmonary Arterial Hypertension

Flolan® (epoprostenol)
Remodulin® (treprostinil)
Tyvaso® (treprostinil)
Veletri® (epoprostenol)
Ventavis® (iloprost)

FDA approval: Various
HCPCS: Flolan/Veletri – J1325; Remodulin –J3285; Tyvaso – J7686; Ventavis - Q4074
Benefit: Pharmacy and Medical

Policy/Criteria:

Note: Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the below criteria are met:
   a) Diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH) confirmed by right heart catherization and not ECHO alone, pulmonary arterial pressure (PAPm) > 25 mmHg
   b) Patient is ≥ 18 years of age
   c) The patient meets the criteria list below depending on the drug/formulation being requested:

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a) Quantity limits are as follows (based on how supplied; refer to background information):

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
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<tbody>
<tr>
<td>epoprostenol (generic)</td>
<td>Highly variable; 20 to 40 ng/kg/min for continuous IV infusion; titrate every 15 minutes</td>
</tr>
<tr>
<td>epoprostenol (Flolan, Veletri®)</td>
<td>same as generic epoprostenol</td>
</tr>
<tr>
<td>iloprost (Ventavis®)</td>
<td>2.5 to 5 mcg nebulized 6 to 9 times per day</td>
</tr>
<tr>
<td>treprostinil (Remodulin®)</td>
<td>Highly variable; 20 to 40 ng/kg/min for continuous SQ or IV infusion; titrate weekly</td>
</tr>
<tr>
<td>treprostinil (Tyvaso®)</td>
<td>54 mcg nebulized four times per day</td>
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</tbody>
</table>

   b) Authorization may be reviewed at least annually to confirm that the medication is effective

Therapeutic considerations:

A. FDA approved indication / Diagnosis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
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<tbody>
<tr>
<td>Flolan®</td>
<td>Treatment of pulmonary arterial hypertension (PAH) (WHO group 1) to improve exercise</td>
</tr>
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</table>

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### Table: Treatment of Pulmonary Arterial Hypertension (PAH)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
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<tbody>
<tr>
<td>(epoprostenol) Veletri&lt;sup&gt;®&lt;/sup&gt; (epoprostenol)</td>
<td>Capacity</td>
</tr>
<tr>
<td>Remodulin&lt;sup&gt;®&lt;/sup&gt; (treprostinil) Tyvaso&lt;sup&gt;®&lt;/sup&gt; (treprostinil)</td>
<td>Treatment of pulmonary arterial hypertension (PAH) (WHO group 1) to diminish symptoms associated with exercise; to diminish the rate of clinical deterioration in patients with PAH requiring transition from epoprostenol</td>
</tr>
<tr>
<td>Ventavis&lt;sup&gt;®&lt;/sup&gt; (iloprost)</td>
<td>For the treatment of pulmonary arterial hypertension (PAH) (WHO group 1) in patients with New York Heart Association (NYHA) class III or IV symptoms to improve exercise tolerance, symptoms, and diminish clinical deterioration</td>
</tr>
</tbody>
</table>

*Please refer to most recent prescribing information.

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**Background Information**

The World Health Organization (WHO) classifies pulmonary hypertension (PH) in five groups, based on underlying etiology of PH. Patients diagnosed with Group 1 pulmonary arterial hypertension (PAH) have generally irreversible disease and may require treatment with PAH-specific therapies. For patients with Groups 2-5, PH may be reversible. Therapy should be directed at treating the underlying cause.

Pharmacologic treatment of PAH includes oral anticoagulants, diuretics, oxygen, inotropic agents (digoxin and dobutamine), calcium channel blockers, prostacyclin and prostacyclin analogs (epoprostenol, treprostinil, and iloprost), endothelin-receptor antagonists (ETAs) (ambrisentan, bosentan, macitentan), PDE-5 inhibitors (sildenafil, tadalafil), and soluble guanylate cyclase stimulators (riociguat).

The place in therapy of individual agents for PAH is not well defined and is typically symptom driven. Generally, a step-wise approach is used to manage patients. In early disease or with less severe symptoms, oral therapies may be used. As symptoms progress, inhaled or injectable therapies, such as epoprostenol, iloprost and treprostinil, become necessary.

Both sildenafil and tadalafil have been studied individually in the treatment of PAH. To date, there is no evidence that either one of these products is more effective than the other. There are currently no trials of sildenafil or tadalafil in patients with Groups 2-5 PH that found improvement in exercise capacity or overall functional status.

Currently, macitentan (Opsumit) is the only oral medication indicated for delaying disease progression and reducing hospitalizations in PAH patients.

**Efficacy**

*Please refer to most recent prescribing information.

**Medication Safety Considerations**

Black Box Warning: No

*Please refer to most recent prescribing information.
E. Dosing and administration

*Please refer to most recent prescribing information.

F. How supplied

a. epoprostenol (generic, Flolan, Veletri): 0.5 mg, 1.5 mg intravenous powder for solution
b. iloprost (Ventavis): 10 mcg/ml, 20 mcg/ml inhalation solution
c. treprostinil (Remodulin): 1 mg/ml, 2.5 mg/ml, 5 mg/ml, 10 mg/ml injection solution
d. treprostinil (Tyvaso): 0.6 mg/ml inhalation solution

References:

10. Marion, DW.  Pulmonary hypertension.  In: UpToDate, Basow, DS (Ed), UptoDate, Waltham, MA, 2013.

<table>
<thead>
<tr>
<th>Policy History</th>
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* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or [http://dailymed.nlm.nih.gov/dailymed/index.cfm](http://dailymed.nlm.nih.gov/dailymed/index.cfm)