Pulmonary Arterial Hypertension (PAH) Treatments

Policy Number: HS-308

Original Effective Date: 10/17/2015

Revised Date(s): 10/6/2016, 8/3/2017

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any. All links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change prior to the annual review date. Lines of business (LOB) are subject to change without notice; current LOBs can be found at www.wellcare.com. All guidelines can be found at this site as well but selecting the Provider tab, then "Tools" and "Clinical Guidelines".

BACKGROUND

Primary pulmonary hypertension (PPH) is a rare but serious, life-threatening disease. As the disease progresses and right ventricular after-load increases, the heart's ability to increase cardiac output with activity declines, resulting in exertional dyspnea, chest pain, or syncpe. Eventually, progressive right heart dysfunction ensues, leading to right heart failure and death. In the National Institutes of Health's PPH registry, the median survival from diagnosis was less than 2.5 years. Medical management consists of anticoagulants, oral vasodilators (which are effective in 20 % to 25 % of cases), continuous intravenous infusions of prostacyclin, diuretics, and supplemental oxygen.1

Clinical Coverage Guideline

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The American College of Chest Physicians guideline and expert panel report on pulmonary hypertension suggests:

1. That the severity of a pulmonary arterial hypertension (PAH) patient's disease be evaluated in a systematic and consistent manner, using a combination of World Health Organization (WHO) functional class (FC), exercise capacity, echocardiographic, laboratory and hemodynamic variables in order to inform therapeutic decisions.

2. Whenever possible, all PAH patients be evaluated promptly at a center with expertise in the diagnosis of PAH, ideally prior to the initiation of therapy.

3. Collaborative and closely coordinated care of PAH patients involving the expertise of both local physicians and those with expertise in PAH care.

Initially, a hospital admission is required to evaluate the patient's pulmonary vascular responsiveness, as this determines selection of vasodilator treatment. Incremental doses of a short-acting pulmonary vasodilator are administered intravenously until a positive hemodynamic response or negative endpoint is observed (e.g., hypotension, headache, chest pain, etc). A decrease of 20 % or more in pulmonary vascular resistance and pulmonary arterial pressure, with no decrease in cardiac output, is considered a positive response.

Responders are usually treated with high doses of oral calcium antagonists (e.g., nifedipine, and diltiazem). Oral calcium antagonists should not be used empirically to treat PAH in the absence of demonstrated acute vasoreactivity.

For treatment naive PAH patients with WHO FC II or WHO FC III symptoms who are not candidates for, or who have failed calcium antagonist therapy, the panel advises monotherapy be initiated with a currently approved endothelin receptor antagonist (ETRA), phosphodiesterase-5 (PDE5) inhibitor, or the soluble guanylate cyclase stimulator riociguat.

The panel suggests also that parenteral or inhaled prostanoids not be chosen as initial therapy for treatment naive PAH patients with WHO FC II symptoms or as second line agents for PAH patients with WHO FC II symptoms who have not met their treatment goals.

For treatment naive PAH patients with WHO FC III symptoms who have evidence of rapid progression of their disease, or other markers of a poor clinical prognosis, the panel advises consideration of initial treatment with a parenteral prostanoid.

For treatment naive PAH patients in WHO FC IV, the panel advises initiation of monotherapy with a parenteral prostanoid agent. For treatment naive PAH patients in WHO FC IV who are unable or do not desire to manage parenteral prostanoid therapy, the panel advises treatment with an inhaled prostanoid in combination with an ETRA.

Continuous intravenous prostaclacin infusions are reserved for those patients who fail to respond to oral calcium antagonists, and may be used either as long-term therapy or as a bridge to transplantation. Because of prostacyclin's very short half-life, it must be administered by continuous infusion by a portable, battery-operated syringe pump through a permanent central venous catheter.

For WHO FC III or IV PAH patients with unacceptable clinical status despite established PAH-specific monotherapy, the panel advises addition of a second class of PAH therapy to improve exercise capacity. Such patients are ideally evaluated at centers with expertise in the evaluation and treatment of complex patients with PAH.

The American College of Cardiology/American Heart Association's expert consensus document on pulmonary hypertension stated that "multiple randomized controlled trials of combination therapy are currently ongoing, and to adequately study the safety and efficacy of combination therapy, we encourage enrollment into randomized controlled trials".

The U.S. Food and Drug Administration (FDA) approved the following infusion and inhalation prostacyclin analogues for use in pulmonary arterial hypertension:

- Epoprostenol (Veletri®, Actelion Pharmaceuticals US, Inc., South San Francisco, CA);
- Epoprostenol sodium (Flolan®, GlaxoSmithKline, Research Triangle Park, NC);
- Iloprost (Ventavis®, Actelion Pharmaceuticals US, Inc., South San Francisco, CA);
Treprostinil (Remodulin® and Tyvaso®, United Therapeutics Corporation, Research Triangle Park, NC).

Side effects most commonly reported with the use of intravenous (IV) epoprostenol or treprostinil than placebo include headache, jaw pain, diarrhea, abdominal pain, anorexia, vomiting, photosensitivity, cutaneous flushing, and arthralgias. Other adverse effects include infection of the catheter site, catheter-related bloodstream infection and sepsis, and malfunction of the drug-delivery system. Site pain occurs frequently in those on subcutaneous treprostinil. Inhaled prostanoids result in cough, headache, flushing, nausea, and syncope more commonly than placebo with iloprost and cough, headache, and flushing more commonly than placebo with treprostinil.

**POSITION STATEMENT**

**Applicable To:**
- Medicaid
- Medicare

**Exclusions**

Use of epoprostenol, treprostinil or iloprost is considered not medically necessary as a treatment for members appropriate for treatment with calcium channel blockers:

- Members who demonstrate a favorable acute hemodynamic response to vasodilators at cardiac catheterization who are deemed appropriate by the treating physician for a trial of calcium channel blocker treatment; **OR**
- Members who demonstrated a favorable acute hemodynamic response to vasodilators but have not become refractory to, or unable to, tolerate therapeutic doses of calcium channel antagonists.

Continuous intravenous infusion of treprostinil sodium (Remodulin) is considered not medically necessary for treatment of individuals when inability to tolerate treatment by subcutaneous infusion has not been documented.

The use of epoprostenol, treprostinil, or iloprost is considered investigational and not medically necessary for all other applications in the absence of WHO Group I PAH including those with WHO Group II to V* pulmonary hypertension and for other causes of pulmonary hypertension, including, but not limited to, left ventricular failure, left sided valvular heart disease, chronic pulmonary diseases, and alveolar hypoventilation syndromes.

**Coverage**

Criteria for members with a diagnosis of Pulmonary Arterial Hypertension (PAH) include:

- Right heart catheterization showing a mean pulmonary artery pressure (mPAP) \(\geq\)25 mm Hg; **AND**
- A pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg; **AND**
- A pulmonary vascular resistance (PVR) greater than 3 Wood units.

A favorable response is defined as a fall in mPAP of at least 10 mm Hg to an absolute mPAP of less than 40 mm Hg without a decrease in cardiac output, when challenged with inhaled nitric oxide, intravenous epoprostenol or intravenous adenosine.

WellCare considers continuous intravenous infusion of epoprostenol sodium (prostacyclin, PGI2, Veletri, Flolan) **medically necessary** as a treatment for individuals who meet all of the following criteria:

- Meets the diagnostic criteria for PAH (above); **AND**
- Demonstrates an unfavorable acute response to vasodilators or is not a candidate for vasodilatory treatment.
In addition, the member must meet one of the following:

- Second line agents for PAH patients with WHO FC II symptoms who have not met their treatment goals OR for treatment naive PAH patients with WHO FC III/IV symptoms who have evidence of rapid progression of their disease, or other markers of a poor clinical prognosis; OR

- Member meets one of the following selection criteria with New York Heart Association Functional Class III or IV symptoms:
  - World Health Organization (WHO) Group I* idiopathic pulmonary arterial hypertension including all subtypes of WHO Group I PAH; OR
  - Pulmonary hypertension associated with connective tissue disorders (e.g., scleroderma, systemic sclerosis, etc.); OR
  - Pulmonary hypertension associated with congenital heart defects.

Continuous subcutaneous infusion of treprostinil sodium (Remodulin) is considered medically necessary as a treatment for individuals who meet all of the following criteria:

- Meets the diagnostic criteria for PAH (above); AND
- Demonstrates an unfavorable acute response to vasodilators or is not a candidate for vasodilatory treatment.

In addition, the member must meet one of the following:

- Second line agents for PAH patients with WHO FC II symptoms who have not met their treatment goals OR for treatment naive PAH patients with WHO FC III/IV symptoms who have evidence of rapid progression of their disease, or other markers of a poor clinical prognosis; OR

- Meets one of the following selection criteria with New York Heart Association functional Class II, III, or IV symptoms:
  - World Health Organization (WHO) Group I* idiopathic pulmonary arterial hypertension including all subtypes of WHO Group I PAH; OR
  - Pulmonary hypertension associated with connective tissue disorders (for example, scleroderma, systemic sclerosis, etc.); OR
  - Pulmonary hypertension associated with congenital heart defects.

Continuous intravenous infusion of treprostinil sodium (Remodulin) is considered medically necessary for treatment of individuals who meet criteria for treprostinil treatment above when there is documented inability to tolerate treatment by subcutaneous infusion.

Inhalation therapy with iloprost (Ventavis) inhalation solution or Tyvaso inhalation solution* (treprostinil) is considered medically necessary as a treatment for individuals who meet all of the following criteria:

- Meets the diagnostic criteria for PAH (above); AND
- Demonstrates an unfavorable acute response to vasodilators or is not a candidate for vasodilatory treatment.

In addition, the member must meet one of the following:

- Second line agents for PAH patients with WHO FC II symptoms who have not met their treatment goals OR for treatment naive PAH patients with WHO FC III/IV symptoms who have evidence of rapid progression of their disease, or other markers of a poor clinical prognosis OR

- Meets one of the following selection criteria with New York Heart Association (NYHA) Functional Class III or IV symptoms:
  - World Health Organization (WHO) Group I* idiopathic pulmonary arterial hypertension including all subtypes of WHO Group I PAH; OR
  - Pulmonary hypertension associated with connective tissue disorders (for example, scleroderma, systemic sclerosis, etc.); OR
  - Pulmonary hypertension associated with congenital heart defects.
PULMONARY ARTERIAL HYPERTENSION (PAH) TREATMENTS
HS-308

CODING

Covered CPT Codes – This list may not be all inclusive
96365 Intravenous and subcutaneous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366 Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96367 Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion of a new drug/substance, up to 1 hour (List separately in addition to code for primary procedure)
96368 Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); concurrent infusion (List separately in addition to code for primary procedure)
96369 Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); initial, up to 1 hour, including pump set-up and establishment of subcutaneous infusion site(s)
96370 Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96371 Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); additional pump set-up with establishment of new subcutaneous infusion site(s) (List separately in addition to code for primary procedure)

Covered HCPCS Codes – This list may not be all inclusive
J1325 Injection, epoprostenol, 0.5 mg
J3285 Injection, treprostinil, 1 mg
J7686 Treprostinil, inhalation solution, FDA-approved final product, non-compounded, administered through DME, unit dose form, 1.74 mg
K0455 Infusion pump used for uninterrupted parenteral administration of medication, (e.g., epoprostenol or treprostinil)
K0730 Controlled dose inhalation drug delivery system
Q4074 Iloprost, inhalation solution, FDA-approved final product, non-compounded, administered through DME, unit dose form, up to 20 micrograms
S0155 Sterile diluant for epoprostenol, 50ml
S9347 Home infusion therapy, uninterrupted, long-term, controlled rate intravenous or subcutaneous infusion therapy (e.g. epoprostenol); administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

Covered ICD-10-CM Diagnosis – This list may not be all inclusive
I26.09 Other pulmonary embolism with acute cor pulmonale
I27.0 Primary pulmonary hypertension [not covered for pulmonary artery denervation]
I27.2 Other secondary pulmonary hypertension

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal / state laws.

REFERENCES

MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

<table>
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<td>Approved by MPC. No changes.</td>
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<tr>
<td>10/17/2015</td>
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