CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Pulmonary Arterial Hypertension – Treprostinil Injection Utilization Management Medical Policy

- Remodulin® (treprostinil subcutaneous or intravenous infusion – United Therapeutics, generic)

REVIEW DATE: 03/04/2026

OVERVIEW

Treprostinil injection, a prostacyclin vasodilator, is indicated for the treatment of pulmonary arterial hypertension (PAH) World Health Organization (WHO) Group 1 to:[1,2]

- **Diminish symptoms associated** with exercise.
- **Reduce the rate of clinical deterioration** for patients who require transition from epoprostenol.

Treprostinil injection has been used with varying results in patients with chronic thromboembolic pulmonary hypertension (CTEPH).[3-7] Benefits noted include improvement in functional class, six-minute walk distance, and in hemodynamic parameters. Treprostinil injection is sometimes used as a bridge prior to surgery. Limited options are available for patients with CTEPH.

Disease Overview

PAH is a serious but rare condition impacting fewer than 20,000 patients in the US.[8,9] It is classified within Group 1 pulmonary hypertension among the five different groups that are recognized. In this progressive disorder the small arteries in the lungs become narrowed, restricted, or blocked causing the heart to work harder to pump blood, leading to activity impairment. Although the mean age of diagnosis is between 36 and 50 years, patients of any age may be affected, including pediatric patients. PAH is defined as a mean pulmonary artery pressure (mPAP) > 20 mmHg (at rest) with a pulmonary arterial wedge pressure (PAWP) ≤ 15 mmHg and a pulmonary vascular resistance > 2 Wood units measured by cardiac catheterization.[14] The prognosis in PAH has been described as poor, with the median survival being approximately 3 years. However, primarily due to advances in pharmacological therapies, the long-term prognosis has improved.

CTEPH is a persistent obstruction of pulmonary arteries and is often a complication of pulmonary embolism.[10,11] It is classified within Group 4 pulmonary hypertension. Symptoms include progressive dyspnea on exertion, as well as fatigue, syncope, hemoptysis, and signs of right heart failure. Pulmonary endarterectomy is the treatment of choice for most patients with CTEPH. However, around 40% of patients are deemed inoperable for various reasons. Medication therapy may also be recommended. Anticoagulant therapy is also given.

Guidelines

Several guidelines address treprostinil injection in the management of pulmonary hypertension.[9,12]

- **Pulmonary Arterial Hypertension:** An updated CHEST guideline and Expert Panel Report regarding therapy for PAH in adults (2019) provides the evidence for use of the many medications for this condition.[9] In the absence of contraindications, patients with PAH should undergo acute vasoreactivity testing utilizing a short-acting agent (e.g., calcium channel blockers). For patients in Functional Class II, oral therapies are recommended such as endothelin receptor antagonists (ambrisentan, bosentan, Opsumit® [macitentan tablets]), phosphodiesterase type 5 inhibitors (tadalafil, sildenafil), and Adempas® (riociguat tablets). It is suggested that parenteral or inhaled

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prostanoids not be chosen as initial therapy for treatment naïve patients with PAH with WHO Functional Class II symptoms or as second-line agents for patients with PAH with WHO Functional Class II who have not met their treatment goals. Prostanoids may be considered in patients who have contraindications or difficulty tolerating phosphodiesterase type 5 inhibitors or endothelin receptor antagonists. Parenteral prostanoids are recommended for patients with PAH in Functional Class III and IV. The European Society of Cardiology (ESC) and the European Respiratory Society (ERS) guidelines regarding the treatment of pulmonary hypertension (2022) also recognize parenteral treprostinil as having a prominent role in the management of this condition, usually in later therapy stages and after other therapies.[12] A simplified treatment algorithm that utilizes risk classifications was introduced in these guidelines and reaffirmed in the 2024 World Symposium on Pulmonary Hypertension.[15] An initial risk assessment is recommended at baseline, 3-4 months, and periodically thereafter; it is based on functional class, 6-minute walk distance, and natiuretic peptides. Hemodynamics and right ventricle imaging can be used to supplement this assessment. For initial risk assessments patient are classified as not high risk or high risk. Patients who are not high risk are recommended to receive a combination of ERAs and PDE-5 inhibitors, whereas those who are high risk may require intravenous or subcutaneous therapies. For follow-up risk assessments, patients are classified into four categories: low-risk, intermediate-low risk, intermediate-high risk, and high risk. Recommendations are made for the addition of an activin-signaling inhibitor (Winrevair [sotatercept-csrk subcutaneous injection]), oral or inhaled prostacyclin therapies, or the switch to a soluble guanylyl cyclase stimulator (sGCS) [Adempas {riociguat tablets}. Patients who are classified as persistent intermediate-high or high-risk may need maximal four-drug therapies and a lung transplant evaluation.

- **Chronic Thromboembolic Pulmonary Hypertension:** Guidelines from the ESC/ERS regarding the treatment of pulmonary hypertension (2022) recommended to consider parenteral prostacyclin analogs for patients with inoperable CTEPH.[12]

Safety

Treprostinil injection should not be abruptly discontinued or have the dose rapidly decreased as rebound pulmonary hypertension may occur.[1,2]

Policy Statement

Prior Authorization is recommended for medical benefit coverage of treprostinil injection. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for 1 year in duration unless otherwise noted below. Specifically, approvals will remain up to 14 days for patients currently receiving the agent for the indication of PAH (WHO Group 1) with inadequate information or if the criteria are not met. These cases are reviewed by a nurse or pharmacist. Because of the specialized skills required for evaluation and diagnosis of patients treated with treprostinil injection as well as the monitoring required for adverse events and long-term efficacy, approval requires treprostinil injection to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: In the *Pulmonary Arterial Hypertension – Treprostinil Injection Utilization Management Medical Policy*, documentation is required for initiation of therapy where noted in the criteria as **[documentation required]**. All documentation must include patient-specific identifying information. Documentation may include, but is not limited to, chart notes and catheterization laboratory results. For a patient case in which the documentation requirement of the right heart catheterization upon Prior

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Authorization coverage review for a different medication indicated for WHO Group 1 PAH has been previously provided, the documentation requirement in this *Pulmonary Arterial Hypertension – Treprostinil Injection Utilization Management Medical Policy* is considered to be met.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of treprostinil injection is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Pulmonary Arterial Hypertension (PAH) World Health Organization (WHO) Group 1.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient has a diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH); AND
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has had a right heart catheterization **[documentation required]** (see documentation section above); AND
       - **b)** Results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
     - **iii.** Patient meets ONE of the following (a or b):
       - **a)** According to the prescriber, patient is intermediate-high risk or high risk; OR
       - **b)** According to the prescriber, patient is low-risk or intermediate-low risk and has tried or is currently receiving one or more agents for PAH from the following different categories (either alone or in combination with another therapy) for ≥ 60 days ([1], [2], [3]. [4], or [5]):
         - **(1)** Phosphodiesterase type 5 (PDE5) inhibitors; OR
         - **(2)** Endothelin receptor antagonists (ERAs); OR
         - **(3)** Adempas (riociguat tablets); OR
         - **(4)** Winrevair (sotatercept-csrk subcutaneous injection); OR
         - **(5)** Prostacyclin analogs/mimetics; AND

         Note: Examples of phosphodiesterase type 5 (PDE5) inhibitors include sildenafil and tadalafil. Endothelin receptor antagonists (ERAs) include bosentan, ambrisentan, Opsumit {macitentan tablets. Prostacyclin analogs/mimetics include Tyvaso (treprostinil inhalation solution), Tyvaso DPI (treprostinil oral inhalation powder), treprostinil injection, epoprostenol injection, Uptravi (selexipag tablets) and Yutrepia (treprostinil inhalation powder).
     - **iv.** Patient with idiopathic PAH must meet ONE of the following (a, b, c, d, or e):
       - **a)** Patient meets BOTH of the following [(1) and (2)]:
         - **(1)** According to the prescriber, the patient has had an acute response to vasodilator testing that occurred during the right heart catheterization; AND

           Note: An example of a response can be defined as a decrease in mean pulmonary artery pressure of at least 10 mm Hg to an absolute mean pulmonary artery pressure of less than 40 mm Hg without a decrease in cardiac output.
         - **(2)** Patient has tried one calcium channel blocker (CCB) therapy; OR

           Note: Examples of CCBs include amlodipine and nifedipine extended-release tablets.

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b) According to the prescriber, the patient did not have an acute response to vasodilator testing; OR
c) According to the prescriber, the patient cannot undergo a vasodilator test; OR
d) Patient cannot take CCB therapy; OR
Note: Examples of reasons patients cannot take CCB therapy include right heart failure or decreased cardiac output.
e) Patient has tried one CCB; AND
Note: Examples of CCBs include amlodipine and nifedipine extended-release tablets.
v. Medication is prescribed by or in consultation with a cardiologist or a pulmonologist; OR

B) Patient Currently Receiving Treprostinil Injection. Approve for the duration noted below if the patient meets ONE of the following (i or ii):
i. Approve for 1 year if the patient meets ALL of the following (a, b, and c):
a) Patient has a diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH); AND
b) Patient meets BOTH of the following [(1) and (2)]:
(1) Patient has had a right heart catheterization; AND
Note: This refers to prior to starting therapy with a medication for WHO Group 1 PAH.
(2) Results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
c) Medication is prescribed by or in consultation with a cardiologist or a pulmonologist; OR
ii. Approve a short-term supply of treprostinil injection for up to 14 days if the patient does not meet the criteria in 1Bi above or if there is insufficient information available. All approvals are reviewed by a nurse or pharmacist.
Note: A 14-day supply should be sufficient to address coverage issues. However, multiple short-term approvals are allowed if a coverage determination cannot be made. Abrupt discontinuation of treprostinil injection therapy may have severe adverse consequences.

Dosing. Approve up to 100 ng/kg/minute given subcutaneously or intravenously.

Other Use with Supportive Evidence

2. **Chronic Thromboembolic Pulmonary Hypertension (CTEPH).** Approve for 1 year if prescribed by or in consultation with a pulmonologist or a cardiologist.

   Dosing. Approve up to 50 ng/kg/minute subcutaneously or intravenously.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of treprostinil injection is not recommended in the following situations:

1. **Chronic Obstructive Pulmonary Disease (COPD) in a Patient Without PAH (WHO Group 1).** COPD is classified as Group 3 Pulmonary Hypertension (pulmonary hypertension associated with lung diseases and/or hypoxia). Pulmonary hypertension may develop late in the course of COPD, but medications used for the treatment of PAH (WHO Group 1) are not recommended therapies.[12]

2. **Concurrent Use with Parenteral Epoprostenol Products, Oral Prostacyclin Products, or Inhaled Prostacyclin Agents Used for Pulmonary Hypertension.**

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Note: Examples of medications include Orenitram (treprostinil extended-release tablets), Uptravi (selexipag tablets and intravenous infusion), Tyvaso (treprostinil inhalation solution), Tyvaso DPI (treprostinil oral inhalation powder),, and epoprostenol intravenous infusion (Flolan, Veletri, generic).

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Pulmonary Arterial Hypertension (PAH) World Health Organization (WHO) Group 1:** For a patient currently receiving treprostinil, added a Note to indicate that requirement of a right heart catheterization (RHC) refers to a RHC prior to starting therapy with a medication for WHO Group 1 PAH.	10/09/2024
Annual Revision	**Pulmonary Arterial Hypertension (PAH) World Health Organization (WHO) Group 1:** For initial therapy, Orenitram (treprostinil extended-release tablets), and Uptravi (selexipag tablets) were removed from the Note of examples of oral medications that the patient has tried or is currently receiving for the condition in Functional Class II.	10/08/2025
Early Annual Revision	**Pulmonary Arterial Hypertension (PAH) World Health Organization (WHO) Group 1:** The requirement that the patient is in Functional Class II, III, or IV was removed. A requirement that, according to the prescriber, the patient is intermediate or high-risk or is low-risk or intermediate-low risk was added. For a patient with low-risk or intermediate-low risk, a requirement and associated Note was added that the patient has tried or is currently receiving one or more agents from the following different categories (either alone or in combination with another therapy) for ≥ 60 days: phosphodiesterase type 5 (PDE5) inhibitors, endothelin receptor antagonists (ERAs), Adempas, Winrevair, or prostacyclin analogs/mimetics. The previous requirement for systemic therapy that applied to all patients with Class II disease was removed. **Conditions Not Recommended for Approval:** Ventavis was removed from the Note that lists examples of medications that should not be taken in combination with treprostinil products.	03/04/2026

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