Drug Coverage Policy

Effective Date.....12/1/2025
Coverage Policy Number.....IP0757
Policy Title.....Treprostinil Injection

Pulmonary Arterial Hypertension – Treprostinil Injection

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

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

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] The estimated incidence of PAH is 2 cases per 1 million per year with a prevalence of 10.6 cases per 1 million adults.[8] It is classified within Group 1 pulmonary hypertension among the five different groups that are recognized.[8,9] 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. In time, right-sided heart failure and/or death may occur. Common PAH symptoms include shortness of breath, fatigue, chest pain, dizziness, and fainting, along with impairment in activity tolerance. It is more prevalent in women. Patients of all ages may develop the disease; however, the mean age of diagnosis typically happens between 36 to 50 years. Children may also have PAH. The condition may occur due to various underlying medical conditions or as a disease (e.g., connective tissue disease, HIV) that uniquely impacts the pulmonary circulation; both genetic and environmental factors may be involved. 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. Lung transplantation may be recommended if pharmacological or medical therapies fail, based upon patient status. The WHO categorizes PAH into stages, which is also referred to as the functional class (Class I to IV) and is an adaptation of the New York Heart Association system to evaluate activity tolerance.

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 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.[9] 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]

- **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]

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of treprostinil injection. 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*, 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 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* is considered to be met.

Treprostinil injection is considered medically necessary when ONE of the following is met (1 or 2):

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, v and vi):
     - **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)** Patient is in Functional Class III or IV; OR
- **b)** Patient is in Functional Class II and meets ONE of the following [(1) or (2)]:
  - **(1)** Patient has tried or is currently receiving one oral agent for PAH; OR
    Note: Examples of oral agents for PAH include bosentan, ambrisentan, Opsumit (macitentan tablets), Opsynvi (macitentan/tadalafil tablets), Adempas (riociguat tablets), sildenafil, tadalafil, Alyq (tadalafil tablets), Tadliq (tadalafil oral suspension).
  - **(2)** Patient has tried one inhaled or parenteral prostacyclin product for PAH; AND
    Note: Examples of inhaled and parenteral prostacyclin products for PAH include Ventavis (iloprost inhalation solution), Tyvaso (treprostinil inhalation solution), Tyvaso DPI (treprostinil oral inhalation powder), Yutrepia (treprostinil oral inhalation powder), and epoprostenol intravenous infusion (Flolan, Veletri, generics).

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.
- **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 a patient 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; AND

vi. Preferred product criteria is met for the product(s) as listed in the below table(s); 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.

Other Uses 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.

Employer Plans and Individual and Family Plans:

Product	Criteria
Remodulin (treprostinil)	Patient meets one of the following (A or B): **A.** Initial therapy: Patient meets one of the following (i or ii): **i.** The patient has tried generic treprostinil; OR **ii.** Patient meets BOTH of the following (a and b): **a.** The request is for Remodulin for continuous subcutaneous infusion; AND **b.** Patient cannot take generic treprostinil because appropriate durable medical equipment is not available such as the patient does not have or cannot obtain a compatible pump that allows generic treprostinil to be administered; OR **B.** Patient has already been started on Remodulin or treprostinil therapy

Conditions Not Covered

Treprostinil injection for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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.[13]

2. **Concurrent Use with Parenteral Epoprostenol Products, Oral Prostacyclin Products, or Inhaled Prostacyclin Agents Used for Pulmonary Hypertension.** 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), Ventavis (iloprost inhalation solution), and epoprostenol intravenous infusion (Flolan, Veletri, generic).

Coding Information

1) This list of codes may not be all-inclusive.

2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3285	Injection, treprostinil, 1 mg

References

1. Remodulin® subcutaneous or intravenous infusion [prescribing information]: Research Triangle Park, NC: United Therapeutics; October 2023.
2. Treprostinil subcutaneous or intravenous infusion [prescribing information]. Princeton, NJ: Sandoz; April 2023.
3. Lang I, Gomez-Sanchez M, Kneussl M, et al. Efficacy of long-term subcutaneous treprostinil sodium therapy in pulmonary hypertension. *CHEST*. 2006;129:1636-1643.
4. Jensen KW, Kerr KM, Fedullo PF, et al. Pulmonary hypertensive medical therapy in chronic thromboembolic pulmonary hypertension before pulmonary thromboendarterectomy. *Circulation*. 2009;120:1248-1254.
5. Skoro-Sajer N, Bonderman D, Wiesbauer F, et al. Treprostinil for severe inoperable chronic thromboembolic pulmonary hypertension. *J Thromb Haemost.* 2006;5:483-489.
6. Sadushi-Kolici R, Jansa P, Kopec G, et al. Subcutaneous treprostinil for the treatment of severe non-operable chronic thromboembolic pulmonary hypertension (CTREPH): a double-blind, phase 3, randomized controlled trial. *Lancet Respir Med*. 2019;7(3):239-248.
7. Sadushi-Kolici R, Lang IM. Treprostinil for the treatment of chronic thromboembolic pulmonary hypertension. *Expert Rev Respir Med*. 2019 Sept 23:1-7.
8. Ruopp NF, Cockrill BA. Diagnosis and treatment of pulmonary arterial hypertension. A review. *JAMA*. 2022;327(14):1379-1391.
9. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for pulmonary arterial hypertension in adults. Update of the CHEST guideline and Expert Panel Report. *CHEST*. 2019;155(3):565-586.
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11. Papamatheakis DG, Poch DS, Fernandes TM, et al. Chronic thromboembolic pulmonary hypertension: JACC focus seminar. *J Am Coll Cardiol*. 2020;76(180):2155-2169.
12. Humbert M, Kovacs G, Hoeper MM, et al, for the ESC/ERS Scientific Document Group. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022 Aug 26. [Online ahead of print].
13. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2024 report). © 2024 Global Initiative for Chronic Obstructive Lung Disease. Available at: https://goldcopd.org/2024-gold-report/. Accessed on October 2, 2024.
14. Maron BA. Revised Definition of Pulmonary Hypertension and Approach to Management: A Clinical Primer. *J Am Heart Assoc*. 2023 Apr 18;12(8):e029024. [Epub].

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy.	11/15/2025

Selected 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.	12/1/2025

The policy effective date is in force until updated or retired.