POLICY Document for treprostinil-Remodulin

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

CAREFIRST: EXCEPTIONS CRITERIA
PULMONARY ARTERIAL HYPERTENSION (PAH) INTRAVENOUS

PREFERRED PRODUCT: TREPROSTINIL INTRAVENOUS INJECTION (generic)

Client Requested: The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the intravenous pulmonary arterial hypertension (PAH) products specified in this policy. Coverage for targeted product is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Intravenous Pulmonary Arterial Hypertension Products

	Product(s)

Preferred*	• **treprostinil** intravenous injection (generic)
Targeted	• **Remodulin** (treprostinil) intravenous injection

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for the targeted product is provided when the following criteria is met:

A. Member has a documented inadequate response, contraindication, or intolerable adverse event to the preferred product and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.

Section 2: Clinical Criteria

Specialty Guideline Management treprostinil-Remodulin

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name	Dosage Form
Remodulin	treprostinil	injection solution

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1,2]

Treatment of pulmonary arterial hypertension (PAH; World Health Organization [WHO] Group 1) to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with New York Heart Association (NYHA) Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH, PAH associated with congenital systemic-to-pulmonary shunts, or PAH associated with connective tissue diseases.

In patients with PAH requiring transition from epoprostenol, to diminish the rate of clinical deterioration. Consider the risks and benefits of each drug prior to transition.

All other indications are considered experimental/investigational and not medically necessary.

Prescriber Specialties

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

Coverage Criteria

Pulmonary Arterial Hypertension (PAH)[1-6]

Indefinite authorization may be granted for treatment of PAH when ALL of the following criteria are met:

- Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- PAH was confirmed by either of the folowing:
  - Pretreatment right heart catheterization with all of the following results:
    - Mean pulmonary arterial pressure (mPAP) > 20 mmHg
    - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
    - Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric members, pulmonary vascular resistance index (PVRI) > 3 Wood units x m^2 is also acceptable.
  - For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

Continuation of Therapy

Indefinite authorization may be granted for members with an indication listed in the coverage criteria section who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

Appendix

WHO Classification of Pulmonary Hypertension (PH)[4]

Note: Patients with heritable PAH or PAH associated with drugs and toxins might be long-term responders to calcium channel blockers.

Group 1: Pulmonary Arterial Hypertension (PAH)

- Idiopathic
  - Long-term responders to calcium channel blockers
- Heritable
- Associated with drugs and toxins
- Associated with:
  - Connective tissue disease
  - Human immunodeficiency virus (HIV) infection
  - Portal hypertension
  - Congenital heart disease
  - Schistosomiasis
- PAH with features of venous/capillary (pulmonary veno-occlusive disease [PVOD]/pulmonary capillary hemangiomatosis [PCH]) involvement
- Persistent PH of the newborn

Group 2: PH associated with Left Heart Disease

Heart failure:
- With preserved ejection fraction
- With reduced or mildly reduced ejection fraction
- Cardiomyopathies with specific etiologies (i.e., hypertrophic, amyloid, Fabry disease, and Chagas disease)

Valvular heart disease:
- Aortic valve disease
- Mitral valve disease
- Mixed valvular disease

Congenital/acquired cardiovascular conditions leading to post-capillary PH

Group 3: PH associated with Lung Diseases and/or Hypoxia

Chronic obstructive pulmonary disease (COPD) and/or emphysema
Interstitial lung disease
Combined pulmonary fibrosis and emphysema
Other parenchymal lung diseases (i.e., parenchymal lung diseases not included in Group 5)
Nonparenchymal restrictive diseases:
- Hypoventilation syndromes
- Pneumonectomy

Hypoxia without lung disease (e.g., high altitude)
Developmental lung diseases

Group 4: PH associated with Pulmonary Artery Obstructions

- Chronic thromboembolic PH
- Other pulmonary artery obstructions:
  - Sarcomas (high- or intermediate-grade or angiosarcoma)
  - Other malignant tumors (e.g., renal carcinoma, uterine carcinoma, germ-cell tumors of the testis)
  - Non-malignant tumors (e.g., uterine leiomyoma)
  - Arteritis without connective tissue disease
  - Congenital pulmonary artery stenoses
  - Hydatidosis

Group 5: PH with Unclear and/or Multifactorial Mechanisms

- Hematological disorders, including inherited and acquired chronic hemolytic anemia and chronic myeloproliferative disorders
- Systemic disorders: Sarcoidosis, pulmonary Langerhans cell histiocytosis, and neurofibromatosis type 1
- Metabolic disorders, including glycogen storage diseases and Gaucher disease
- Chronic renal failure with or without hemodialysis
- Pulmonary tumor thrombotic microangiopathy
- Fibrosing mediastinitis
- Complex congenital heart disease

REFERENCES:

SECTION 1

1. Remodulin [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; July 2021.
2. Treprostinil [package insert]. Princeton, NJ: Sandoz Inc.; April 2019.

SECTION 2

1. Remodulin [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; October 2023.
2. Treprostinil [package insert]. Princeton, NJ: Sandoz Inc.; April 2023.
3. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53(1):1801913. doi:10.1183/13993003.01913-2018.
4. Kovacs G, Bartolome S, Denton CP, et al. Definition, classification and diagnosis of pulmonary hypertension. Eur Respir J. 2024;64(4):2401324. doi: 10.1183/13993003.01324-2024
5. Chin KM, Gaine SP, Gerges C, et al. Treatment algorithm for pulmonary arterial hypertension. Eur Respir J. 2024;64(4):2401325. doi: 10.1183/13993003.01325-2024
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