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Section:	Prescription Drugs	**Effective Date:**	October 1, 2024
Subsection:	Cardiovascular Agents	**Original Policy Date:**	June 9, 2011
Subject:	Remodulin	**Page:**	1 of 7

Last Review Date: September 6, 2024

Remodulin

Description

Remodulin (treprostinil)

Background
Pulmonary arterial hypertension is a rare disorder of the pulmonary arteries in which the pulmonary arterial pressure rises above normal levels in the absence of left ventricular failure. This condition can progress to cause right-sided heart failure and death Remodulin is indicated for treatment of pulmonary arterial hypertension (PAH) which is classified by WHO as Group 1. Remodulin is used to treat pulmonary arterial hypertension (PAH, high blood pressure in the lungs) to improve the exercise ability (1).

The World Health Organization (WHO) has classified pulmonary hypertension into five different groups: (2)

WHO Group 1: Pulmonary Arterial Hypertension (PAH)
1.1 Idiopathic (IPAH)
1.2 Heritable PAH
- 1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
- 1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
- 1.2.3 Unknown

1.3 Drug-and toxin-induced
1.4 Associated with:
- 1.4.1 Connective tissue diseases

1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart diseases
1.4.5 Schistosomiasis

1'. Pulmonary vena-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)

1". Persistent pulmonary hypertension of the newborn (PPHN)

The diagnosis of WHO Group 1 PAH requires a right heart catheterization to demonstrate an mPAP ≥ 20mmHg at rest and a pulmonary vascular resistance (PVR) ≥ 3 Wood units, mean pulmonary capillary wedge pressure ≤ 15mmHg (to exclude pulmonary hypertension due to left heart disease, i.e., WHO Group 2 pulmonary hypertension) (4-6).

WHO Group 2: Pulmonary Hypertension Owing to Left Heart Disease

2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3: Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia

3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4: Chronic Thromboembolic Pulmonary Hypertension <CTEPHI

WHO Group 5: Pulmonary Hypertension with Unclear Multifactorial Mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher's disease, thyroid disorders

5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

The American College of Chest Physicians (ACCP) has published an updated clinical practice guideline for treating PAH. These guidelines use the New York Heart Association (NYHA) functional classification of physical activity scale to classify PAH patients in classes I-IV based on the severity of their symptoms (3). Remodulin is indicated for patients with NYHA Functional Class II, III, and IV (1).

Class I	Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.
Class II	Patients with pulmonary hypertension resulting in slight limitation of physical activity. These patients are comfortable at rest, but ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class III	Patients with pulmonary hypertension resulting in marked limitation of physical activity. These patients are comfortable at rest, but less than ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class IV	Patients with pulmonary hypertension resulting in inability to perform any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may be present at rest, and discomfort is increased by any physical activity.

(3)

Regulatory Status

FDA-approved indication: Remodulin is a prostacyclin vasodilator indicated for: (1)

- Treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with NYHA Functional Class II=IV symptoms and etiologies of idiopathic or heritable PAH (58%), PAH associated with congenital systemic-to-pulmonary shunts (23%), or PAH associated with connective tissue diseases (19%).
- Patients who require transition from epoprostenol, to reduce the rate of clinical deterioration. The risks and benefits of each drug should be carefully considered prior to transition.

Adverse reactions reported with Remodulin in over 20% of patients in clinical trials include infusion site pain, infusion site reaction, headache, diarrhea, and nausea (1).

Concomitant administration of Remodulin with diuretics, antihypertensive agents or other

vasodilators may increase the risk of symptomatic hypotension. Since Remodulin inhibits platelet aggregation, there may be an increased risk of bleeding, particularly among patients receiving anticoagulants (1).

Safety and effectiveness in pediatric patients have not been established (1).

Related policies
Adcirca, Adempas, Flolan/Veletri, Letairis, Opsumit, Orenitram, PDE5 Inhibitor powders, Revatio, Tracleer, Tyvaso, Uptravi, Ventavis

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Remodulin may be considered **medically necessary** if the conditions indicated below are met.

Remodulin may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Pulmonary Arterial Hypertension (PAH) - **WHO Group I**
    a. NYHA functional classification of physical activity – **Class II, III, or IV**

2. Transition from Epoprostenol (Flolan/Veletri) to reduce rate of clinical deterioration

AND the following:

1. Prescribed by or recommended by a cardiologist or pulmonologist

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ALL** of the following:

1. Pulmonary Arterial Hypertension (PAH) - **WHO Group I**
2. Symptoms have improved or stabilized

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 2 years

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Pulmonary arterial hypertension is a rare disorder of the pulmonary arteries in which the pulmonary arterial pressure rises above normal levels in the absence of left ventricular failure. This condition can progress to cause heart right failure and death. Remodulin is a prostacyclin vasodilator indicated for treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) in patients with NYHA class II, III, or IV. Remodulin is also indicated for patients who require transition from epoprostenol, to reduce the rate of clinical deterioration. Remodulin has been shown to diminish symptoms associated with exercise. Remodulin is a potent pulmonary and systemic vasodilator formulated for subcutaneous or intravenous administration. Initiation of Remodulin must be performed in a setting with adequate personnel and equipment for physiological monitoring and emergency care (1-3).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Remodulin while maintaining optimal therapeutic outcomes.

References

1. Remodulin [package insert]. Research Triangle Park, NC: United Therapeutics Corp; October 2023.
2. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013; 62:034-841.
3. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest.* 2014; 46(2):449-475.
4. Simonneau G, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53(1) Epub 2019 Jan 24.
5. Rose-Jones LJ and Mclaughlin V. Pulmonary Hypertension: Types and Treatments. Curr Cardiol Rev. 2015 Feb; 11(1): 73–79.
6. Rudolf KF, et al. Usefulness of pulmonary capillary wedge pressure as a correlate of left ventricular filling pressures in pulmonary arterial hypertension. The Journal of Heart and Lung Transplantation, Vol33, No2. February 2014.

Policy History

Date	Action
June 2012	Annual editorial and reference update
March 2013	Annual editorial and reference update
March 2014	Annual review and reference update
June 2016	Annual editorial review and reference update Addition of age 18 Policy number change from 5.06.05 to 5.40.17
September 2017	Annual editorial review
September 2018	Annual review
September 2019	Annual editorial review and reference update. Changed approval duration from lifetime to 2 years
March 2020	Annual review. Revised background section and added initial requirement of prescribed by or recommended by a cardiologist or pulmonologist per SME
September 2021	Annual review and reference update
December 2021	Annual review and reference update
September 2022	Annual review
December 2022	Annual review
September 2023	Annual review
March 2024	Annual review
September 2024	Annual editorial review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.