Treprostinil for Continuous Subcutaneous/Intravenous Infusion (Remodulin®)

NDC CODE(S)

00703-0666-XX TREPROSTINIL 1MG/ML Solution (TEVA PARENTERAL MEDICINES)
00703-0676-XX TREPROSTINIL 2.5MG/ML Solution (TEVA PARENTERAL MEDICINES)
00703-0686-XX TREPROSTINIL 5MG/ML Solution (TEVA PARENTERAL MEDICINES)
00703-0696-XX TREPROSTINIL 10MG/ML Solution (TEVA PARENTERAL MEDICINES)
00781-3420-XX TREPROSTINIL 1MG/ML Solution (SANDOZ)
00781-3425-XX TREPROSTINIL 2.5MG/ML Solution (SANDOZ)
00781-3427-XX TREPROSTINIL 5MG/ML Solution (SANDOZ)
00781-3430-XX TREPROSTINIL 10MG/ML Solution (SANDOZ)
42023-0206-XX TREPROSTINIL 20MG/20ML Solution (PAR STERILE PRODUCTS)
42023-0207-XX TREPROSTINIL 50MG/20ML Solution (PAR STERILE PRODUCTS)
42023-0208-XX TREPROSTINIL 100MG/20ML Solution (PAR STERILE PRODUCTS)
42023-0209-XX TREPROSTINIL 200MG/20ML Solution (PAR STERILE PRODUCTS)
66302-0101-XX REMODULIN 1MG/ML Solution (UNITED THERAPEUTICS CORP)
66302-0102-XX REMODULIN 2.5MG/ML Solution (UNITED THERAPEUTICS CORP)
66302-0105-XX REMODULIN 5MG/ML Solution (UNITED THERAPEUTICS CORP)
66302-0110-X REMODULIN 10MG/ML Solution (UNITED THERAPEUTICS CORP)

DESCRIPTION

Treprostinil is a stable synthetic analog of prostacyclin, a powerful vasodilator and inhibitor of platelet aggregation. Its exact mechanism of vasodilation activity is not known, but prostacyclin synthase expression is decreased in the lungs of individuals with pulmonary arterial hypertension (PAH).

Treprostinil is commercially available for use in three routes of administration: subcutaneous or intravenous infusion and oral inhalation; however this policy exclusively addresses administration by subcutaneous or intravenous infusion.

POLICY

- Treprostinil for continuous subcutaneous or intravenous infusion for the treatment of Pulmonary Arterial Hypertension is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**

- Treprostinil for continuous subcutaneous or intravenous infusion for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Patient is at least 17 years of age for Remodulin®; **AND**

Pulmonary arterial hypertension (PAH)
- Diagnosis confirmed by documented right heart catheterization with **ALL** of the following:
  - Mean pulmonary artery pressure (mPAP) > 20 mm Hg; **AND**
  - Pulmonary arterial wedge pressure (PAWP) ≤ 15 mmHg; **AND**
  - Pulmonary vascular resistance (PVR) ≥ 3 wood units (240 dynes-sec/cm^5); **AND**

- Baseline assessment of 6 minute walk distance (6MWD) and/or B-type natriuretic peptide plasma levels (NT-proBNP); **AND**
- Diagnosed with pulmonary arterial hypertension and classified as WHO (World Health Organization) ~~WHO~~ Group 1 (See below for description of WHO classification for pulmonary hypertension); **AND**
- Designated as New York Heart Association (NYHA) or World Health Organization (WHO) functional class II-IV (See below for description of functional classes); **AND**
- Patient is treatment-naïve to PAH-specific pharmacotherapy §; **AND**
  - Patient is Functional Class III with evidence of rapid progression of their disease, or other markers of a poor clinical prognosis; **AND**
    - Patient will be treated with IV or SC Remodulin®; **OR**
  - Patient is Functional Class IV; **AND**
    - Patient will be treated with IV or SC Remodulin®; **OR**
- Patient is Functional Class III or IV with an inadequate clinical response‡ (see criteria below) to two classes of PAH pharmacotherapy and will be adding a third class of PAH therapy (see PAH pharmacotherapy table below§): **OR**
- Patient is transitioning from Remodulin® to Orenitram® and using Remodulin® (treprostinil) and Orenitram® (treprostinil) concurrently; **OR**
- Patient is transitioning from epoprostenol to Remodulin® (treprostinil)

Pulmonary Hypertension Pharmacotherapy§		
Class	Drug	Route of Administration
Phosphodiesterase-5 inhibitors (PDE5i)	Revatio (Sildenafil) Adcirca (Tadalafil)	IV, Oral Oral
Prostacyclin analogs	Flolan, Veletri (Epoprostenol) Orenitram, Remodulin, Tyvaso (Treprostinil) Ventavis (Iloprost)	IV Oral, IV/SC, Inhaled Inhaled
Endothelial-receptor antagonists (ERA)	Tracleer (Bosentan) Letairis (Ambrisentan) Opsumit (Macitentan)	Oral Oral Oral
Soluble guanylate cyclase stimulators	Adempas (riociguat) Must NOT be used in combination with PDE5i (e.g., Revatio, Adcirca) or intravenous prostacyclin analogs (e.g., Flolan, Veletri, Remodulin) Subcutaneous administration of Remodulin is allowable with Adempas	Oral
Prostacyclin receptor agonists	Uptravi (selexipag) May be used in combination with BOTH a PDE5i AND an ERA	Oral

Inadequate Clinical Response Criteria ‡
• Inadequate clinical response for patients who were initially in WHO Functional Class II or III: ▪ Resulting clinical status defined as stable and not satisfactory; **OR** ▪ Resulting clinical status defined as unstable and deteriorating • Inadequate clinical response for patients who were initially in WHO Functional Class IV: ▪ No rapid improvement to WHO Functional Class III or better; **OR** ▪ Resulting clinical status defined as stable and not satisfactory

Reference charts
WHO Classification of Pulmonary Hypertension (PH): • Group 1 PAH: Pulmonary arterial hypertension (PAH) • Group 2 PH: Pulmonary hypertension owing to left heart disease • Group 3 PH: Pulmonary hypertension owing to lung diseases and/or hypoxia • Group 4 PH: Chronic thromboembolic pulmonary hypertension (CTEPH) • Group 5 PH: Pulmonary hypertension with unclear multifactorial mechanisms
New York Heart Association (NYHA) Functional Classification: • Class I: No symptoms with ordinary physical activity. • Class II: Symptoms with ordinary activity. Slight limitation of activity. • Class III: Symptoms with less than ordinary activity. Marked limitation of activity. • Class IV: Symptoms with any activity or even at rest.
World Health Organization (WHO) Functional Assessment Classification: • Class I: Patients with PH 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 PH resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope. • Class III: Patients with PH resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope • Class IV: Patients with PH with inability to carry out any physical activity without symptoms. These patients manifest signs of right-heart failure. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. in initial approval criteria; **AND**
- Disease response as determined by one or more of the following:
  - Progress towards an improvement in WHO functional class status
  - Improvement in right ventricular function (based on echocardiogram or cardiac MRI)
  - Improvement (from baseline) on the 6 minute walk distance (6MWD)
  - Improvement in B-type natriuretic peptide plasma levels (NT-proBNP); **AND**

Remodulin®

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: catheter-blood stream infections (BSIs), sepsis, severe infusion site reactions, symptomatic hypotension, anticoagulation abnormalities/ risk of bleeding, etc.

INDICATION	DOSE
Remodulin® (Continuous Subcutaneous/ or Intravenous Infusion)	1.25 ng/kg/min (or 0.625 ng/kg/min if not tolerated or in patients with mild or moderate hepatic insufficiency); dose increase based on clinical response (increments of 1.25 ng/kg/min per week for the first 4 weeks of treatment, then 2.5 ng/kg/min per week for the remaining duration of the infusion). **Transitioning from epoprostenol** • Initiate Remodulin at a recommended dose of 10% of the current epoprostenol dose

	• Decrease the dose of epoprostenol while simultaneously increasing the dose of Remodulin, based on response

LENGTH OF AUTHORIZATION

Coverage will be provided for six months and is eligible for renewal.

DOSAGE LIMITS

Max Units (per dose and over time) [HCPC Unit]:

Remodulin®
- 7 billable units per day

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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3. Flolan [package insert]. Research Triangle Park, NC; GlaxoSmithKline; November 2019. Accessed December 2020.
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EFFECTIVE DATE 6/2/2021

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