## Prior Authorization Review Panel

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**CHC-MCO Policy Submission**

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

| | |
|---|---|
| **Plan: PA Health & Wellness** | **Submission Date: 08/01/2021** |
| **Policy Number: PA.CP.PHAR.199** | **Effective Date: 01/2020**<br>**Revision Date: 07/2021** |
| **Policy Name: Treprostinil (Remodulin)** | |

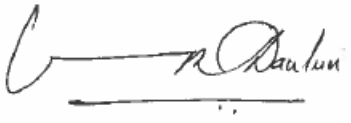
**Type of Submission – Check all that apply:**

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

**Please provide any changes or clarifying information for the policy below:**

1Q 2021 annual review: Revised the example of medical justification supporting inability to use generic Remodulin from "lack of subcutaneous infusion pump access" to "IV administration not suitable and subcutaneous generic Remodulin is not available"; added generic redirection to Section II; added Appendix G; references reviewed and updated.

| | |
|---|---|
| **Name of Authorized Individual (Please type or print):**<br><br>**Venkateswara R. Davuluri, MD** | **Signature of Authorized Individual:**  |

# Clinical Policy: Treprostinil (Remodulin)

Reference Number: PA.CP.PHAR.199
Effective Date: 01/2018
Last Review Date: 07/2021

Coding Implications
Revision Log

**Description**
Treprostinil (Remodulin®) is a prostacyclin analog.

**FDA Approved Indication(s)**
Remodulin are indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability. Remodulin is also indicated to reduce the rate of clinical deterioration in patients with PAH requiring transition from Flolan (epoprostenol sodium). The risks and benefits of each drug should be carefully considered prior to transition.

Studies establishing effectiveness included predominately 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. Nearly all controlled clinical experience with inhaled treprostinil has been on a background of bosentan (an endothelin receptor antagonist) or sildenafil (a phosphodiesterase type 5 inhibitor) with study duration of 12 weeks.

**Policy/Criteria**
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Remodulin is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Pulmonary Arterial Hypertension** (must meet all):

1. Diagnosis of PAH;
2. Prescribed by or in consultation with a cardiologist or pulmonologist;
3. Failure of a calcium channel blocker (*see Appendix B*), unless member meets one of the following (a, b or c):
   a. Inadequate response or contraindication to acute vasodilator testing;
   b. Contraindication or clinically significant adverse effects to calcium channel blockers are experienced;
   c. Members already taking and stabilized on treprostinil will not be required to change therapy;
4. If request is for brand Remodulin, medical justification supports inability to use generic treprostinil (e.g., contraindications to excipients in the generic formulation, or IV administration is not suitable and subcutaneous generic Remodulin is not available) (*see Appendix G)*;

**Approval duration: 6 months**

**B. Other diagnoses/indications:** Refer to PA.CP.PMN.53

## II. Continued Approval

**A. Pulmonary Arterial Hypertension** (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for brand Remodulin, medical justification supports inability to use generic treprostinil (e.g., contraindications to excipients in the generic formulation, or IV administration is not suitable and subcutaneous generic Remodulin is not available) (*see Appendix G)*;

**Approval duration: 12 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; **Approval duration: Duration of request or 12 months (whichever is less)**; or

1. Refer to PA.CP.PMN.53

## III. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

FC: functional class
FDA: Food and Drug Administration
FVC: forced vital capacity
mPAP: mean pulmonary arterial pressure
NYHA: New York Heart Association
PAH: pulmonary arterial hypertension
PCWP: pulmonary capillary wedge pressure
PH: pulmonary hypertension
PVR: pulmonary vascular resistance
WHO: World Health Organization
WU: Wood Units

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| nifedipine (Adalat® CC, Afeditab® CR, Procardia®, Procardia XL®) | 60 mg PO QD; may increase to 120 to 240 mg/day | 240 mg/day |
| diltiazem (Dilacor XR®, Dilt-XR®, Cardizem® CD, Cartia XT®, Tiazac®, Taztia XT®, Cardizem® LA, Matzim® LA) | 720 to 960 mg PO QD | 960 mg/day |
| amlodipine (Norvasc®) | 20 to 30 mg PO QD | 30 mg/day |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - None
- Boxed warnings(s): none reported

*Appendix D: Pulmonary Hypertension: WHO Classification*

- Group 1: PAH (pulmonary arterial hypertension)
- Group 2: PH due to left heart disease
- Group 3: PH due to lung disease and/or hypoxemia
- Group 4: CTEPH (chronic thromboembolic pulmonary hypertension)
- Group 5: PH due to unclear multifactorial mechanisms

*Appendix E: Pulmonary Hypertension: WHO/NYHA Functional Classes (FC)*

| Treatment Approach* | FC | Status at Rest | Tolerance of Physical Activity (PA) | PA Limitations | Heart Failure |
|---|---|---|---|---|---|
| Monitoring for progression of PH and treatment of co-existing conditions | I | Comfortable at rest | No limitation | Ordinary PA does not cause undue dyspnea or fatigue, chest pain, or near syncope. | |
| Advanced treatment of PH with PH-targeted therapy - *see Appendix F*** | II | Comfortable at rest | Slight limitation | Ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope. | |
| | III | Comfortable at rest | Marked limitation | Less than ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope. | |
| | IV | Dyspnea or fatigue may be present at rest | Inability to carry out any PA without symptoms | Discomfort is increased by any PA. | Signs of right heart failure |

*PH supportive measures may include diuretics, oxygen therapy, anticoagulation, digoxin, exercise, pneumococcal vaccination. **Advanced treatment options also include calcium channel blockers.

*Appendix F: Pulmonary Hypertension: Targeted Therapies*

| Mechanism of Action | Drug Class | Drug Subclass | Drug | Brand/Generic Formulations |
|---|---|---|---|---|
| Reduction of pulmonary arterial pressure | Prostacyclin* pathway agonist<br><br>**Member of the prostanoid class* | Prostacyclin | Epoprostenol | Veletri (IV)<br>Flolan (IV)<br>Flolan generic (IV) |
| | | Synthetic prostacyclin analog | Treprostinil | Orenitram (oral tablet) |

| Mechanism of Action | Drug Class | Drug Subclass | Drug | Brand/Generic Formulations |
|---|---|---|---|---|
| through vasodilation | *of fatty acid derivatives.* | | | Remodulin (IV) Tyvaso (inhalation) |
| | | | Iloprost | Ventavis (inhalation) |
| | | Non-prostanoid prostacyclin receptor (IP receptor) agonist | Selexipag | Uptravi (oral tablet) |
| | Endothelin receptor antagonist (ETRA) | Selective receptor antagonist | Ambrisentan | Letairis (oral tablet) |
| | | Nonselective dual action receptor antagonist | Bosentan | Tracleer (oral tablet) |
| | | | Macitentan | Opsumit (oral tablet) |
| | Nitric oxide-cyclic guanosine monophosphate enhancer | Phosphodiesterase type 5 (PDE5) inhibitor | Sildenafil | Revatio (IV, oral tablet, oral suspension) |
| | | | Tadalafil | Adcirca (oral tablet) |
| | | Guanylate cyclase stimulant (sGC) | Riociguat | Adempas (oral tablet) |

*Appendix G: General Information*

- Generic treprostinil injection is approved by the U.S. Food and Drug Administration for both intravenous and subcutaneous use. However, generic treprostinil for subcutaneous use has limited availability of CADD-MS® 3 pump and subcutaneous pump supplies. Patients prescribed generic treprostinil will only be able to use the medication intravenously until an alternative supplier for generic treprostinil subcutaneous delivery devices is identified.
- Patients prescribed branded Remodulin may continue to use the medication both intravenously and subcutaneously, if they have access to the subcutaneous supplies.

## IV. Dosage and Administration

| Drug Name | Dosing Regimen | Maximum Dose |
|---|---|---|
| Treprostinil (Remodulin) | 1.25 ng/kg/min SC or IV; can be increased weekly based on clinical response | Based on weight and tolerability |

## V. Product Availability

| Drug | Availability |
|---|---|
| Treprostinil (Remodulin) | 20 mL vials: 20 mg, 50 mg, 100 mg, 200 mg |

## VI. References

1. Orenitram Prescribing Information. Research Triangle, NC: United Therapeutics Corp.; October 2019. Available at: https://www.orenitram.com. Accessed October 8, 2020.
2. Remodulin Prescribing Information. Research Triangle Park, NC: United Therapeutics Corp.; July 2018. Available at: https://www.remodulin.com. Accessed October 8, 2020.
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9. Simmonneau G, Montani D, Celermajer D, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J*. 2019; 53:1801913.
10. Sitbon O, Humber M, Jais X, et al. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation*. 2005;111(23);3105;11.
11. Generic Treprostinil Injection Launched for Intravenous Use. Pulmonary Hypertension Association. April 2019. Available at: https://phassociation.org/. Accessed August 6, 2020.
12. Yaghi S, Novikov A, Trandafirescu T. Clinical update on pulmonary hypertension. *J Investig Med*. 2020; 0:1-7. doi:10.1136/jim-2020-001291.
13. Waxman A, Restrepo-Jaramillo R, Thenappan T, et al. Inhaled treprostinil in pulmonary hypertension due to interstitial lung disease. *NEJM*. 2021;384:325-34.

## Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| J3285 | Injection, treprostinil, 1mg |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| Removed WHO/NYHA classifications from initial criteria since specialist is involved in care. References reviewed and updated. | 02/18 | |
| Q3 2020: Reintroducing policy for Remodulin; removed criteria pertaining to Orenitram and Tyvaso as these agents are included in the Pennsylvania Medical Assistance Program's Statewide PDL and are subject to the State-directed prior authorization guidelines; references reviewed and updated. | 07/2020 | |
| 1Q 2021 annual review: Revised the example of medical justification supporting inability to use generic Remodulin from "lack of subcutaneous infusion pump access" to "IV administration not suitable and subcutaneous generic Remodulin is not available"; added generic redirection to Section II; added Appendix G; references reviewed and updated. | 07/2021 | |