Clinical Policy: Treprostinil (Remodulin)

Reference Number: PA.CP.PHAR.199
Effective Date: 01/2018
Last Review Date: 07/2023

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 PA Health & 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, member must use generic treprostinil, unless contraindicated or clinically significant adverse effects are experienced.

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 PA Health & 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, member must use generic treprostinil, unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 12 months

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

1. Currently receiving medication via PA Health & 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
2. 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 **Member of the prostanoid class*	Prostacyclin	Epoprostenol	Veletri (IV) Flolan (IV) Flolan generic (IV)
		Synthetic prostacyclin analog	Treprostinil	Orenitram (oral tablet) Remodulin (IV)

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
through vasodilation	*of fatty acid derivatives.*			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)

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. Remodulin Prescribing Information. Research Triangle Park, NC: United Therapeutics Corp.; July 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021272Orig1s032lbl.pdf. Accessed November 18, 2022.
2. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: A report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association - developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009; 53(17): 1573-1619.

3. 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. doi: https://doi.org/10.1016/j.chest.2018.11.030.
4. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: Guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015 Nov 24; 132(21): 2037-99.
5. Kim NH, Delcroix M, Jenkins DP, et al. Chronic thromboembolic pulmonary hypertension. *J Am Coll Cardiol*. 2013; 62(25): Suppl D92-99.
6. Galiè N, Humbert M, Vachiary JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of Pulmonary Hypertension. *European Heart Journal*. Doi:10.1093/eurheartj/ehv317.
7. Simmonneau G, Montani D, Celermajer D, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J*. 2019; 53:1801913.
8. 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.
9. Generic Treprostinil Injection Launched for Intravenous Use. Pulmonary Hypertension Association. April 2019. Available at: https://phassociation.org/. Accessed August 6, 2020.
10. Yaghi S, Novikov A, Trandafirescu T. Clinical update on pulmonary hypertension. *J Investig Med*. 2020; 0:1-7. doi:10.1136/jim-2020-001291.
11. Waxman A, Restrepo-Jaramillo R, Thenappan T, et al. Inhaled treprostinil in pulmonary hypertension due to interstitial lung disease. *NEJM*. 2021;384:325-34.
12. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. European Heart Journal, Volume 43, Issue 38, 7 October 2022, Pages 3618–3731, https://doi.org/10.1093/eurheartj/ehac237.

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.	02/2018	
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	07/2021	

Reviews, Revisions, and Approvals	Date	Approval Date
generic Remodulin is not available"; added generic redirection to Section II; added Appendix G; references reviewed and updated.		
1Q 2022 annual review: removed "or IV administration is not suitable and subcutaneous generic Remodulin is not available" as a pontential exception for generic redirection requirement, as generic SC treprostinil is now available; references reviewed and updated.	07/2022	
1Q 2023 annual review: no significant changes; references reviewed and updated.	07/2023	