Clinical Policy: Treprostinil (Remodulin)

Reference Number: LA.PHAR.199
Effective Date:
Last Review Date: 06.21
Line of Business: Medicaid

Coding Implications Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Treprostinil (Remodulin®) is a prostacyclin analog.

FDA Approved Indication(s)

Remodulin is 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

Prior authorization is required. Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections 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 or b):**
   a. **Inadequate response or contraindication to acute vasodilator testing;**
   b. **Contraindication or clinically significant adverse effects to calcium channel blockers are experienced;**

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);***
5. **Provider must submit treatment plan detailing pump rate, dose, quantity (in mL), and frequency of cassette change;**

Approval duration:
Medicaid – 6 months

B. Other diagnoses/indications
1. **Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.**

II. Continued Therapy

A. Pulmonary Arterial Hypertension (must meet all):
1. **Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met all initial approval criteria;**
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);***
4. **Provider must submit treatment plan detailing pump rate, dose, quantity (in mL) and frequency of cassette change;**

Approval duration:
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2):
1. **Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.**
   Approval duration: Duration of request or 6 months (whichever is less); or
2. **Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.**

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FC: functional class **FDA: Food and Drug Administration**

NYHA: New York Heart Association **PH: pulmonary hypertension**
PAH: pulmonary arterial hypertension **WHO: World Health Organization**

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here 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 reported**

- **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	II	Comfortable at rest	Slight limitation	Ordinary PA causes undue dyspnea or	

Treatment Approach*	FC	Status at Rest	Tolerance of Physical Activity (PA)	PA Limitations	Heart Failure
PH with PH-targeted therapy - *see Appendix F***				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 through vasodilation	Prostacyclin* pathway agonist **Member of the prostanoid class of fatty acid derivatives.*	Prostacyclin	Epoprostenol	Veletri (IV) Flolan (IV) Flolan generic (IV)
		Synthetic prostacyclin analog	Treprostinil	Orenitram (oral tablet) 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	Phosphodiesterase type 5 (PDE5) inhibitor	Sildenafil	Revatio (IV, oral tablet, oral suspension)

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
	monophosphate enhancer		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.**

V. 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

VI. Product Availability

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

VII. References

1. Remodulin Prescribing Information. Research Triangle Park, NC: United Therapeutics Corp.; July 2018. Available at: https://www.remodulin.com. Accessed October 8, 2020.
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.

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.**

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
Converted corporate to local policy	06.2021

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

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