Clinical Policy: Treprostinil (Remodulin)

Reference Number: LA.PHAR.199
Effective Date: 09.29.23
Last Review Date: ~~05.09.23~~04.28.24 Coding Implications
Line of Business: Medicaid Revision Log

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

Please note: This policy is for medical benefit

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.

For PAH, 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
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 treprostinil 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. ~~Member~~If request is for brand Remodulin, member must use generic treprostinil, unless contraindicated or clinically significant adverse effects are experienced;

5. Request meets one of the following:
   a. Remodulin: Provider must submit treatment plan detailing pump rate, dose, quantity (in mL), and frequency of cassette change;

Approval duration: 6 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

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II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member must use generic treprostinil, unless contraindicated or clinically significant adverse effects are experienced;
4. Request meets one of the following:
   a. Remodulin: Provider must submit treatment plan detailing pump rate, dose, quantity (in mL) and frequency of cassette change;

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 policies – LA.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CTEPH: chronic thromboembolic pulmonary hypertension
FC: functional class
FDA: Food and Drug Administration
FVC: forced vital capacity
mPAP: mean pulmonary arterial pressure
NYHA: New York Heart Association
PA: physical ability
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 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

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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 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, Tyvaso DPI (inhalation)
			Iloprost	Ventavis (inhalation)
		Non-prostanoid prostacyclin receptor (IP receptor) agonist	Selexipag	Uptravi (oral tablet)
	Endothelin receptor	Selective receptor antagonist	Ambrisentan	Letairis (oral tablet)

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
	antagonist (ETRA)	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)

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 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021272Orig1s032lbl.pdf. Accessed November 18, 2022.
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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

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Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.09.23	08.28.23
Annual review: no significant changes; clarified wording surrounding the preference for generic Remodulin; references reviewed and updated.	04.28.24	

Important Reminder

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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. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and

limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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