Clinical Policy: Treprostinil (Orenitram, Remodulin, Tyvasco)

Reference Number: CP.PHAR.199
Effective Date: 03/16
Last Review Date: 03/17

Coding Implications
Revision Log

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for treprostinil (Orenitram®, Remodulin®, Tyvaso®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Orenitram, Remodulin, Tyvaso are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pulmonary Hypertension (must meet all):

1. Prescribed by or in consultation with a cardiologist or pulmonologist experienced in the diagnosis and treatment of pulmonary hypertension (PH);
2. Diagnosis of PH confirmed by right heart catheterization and classified as (a and b):
   a. WHO Group 1: PAH (pulmonary arterial hypertension; Appendix B) and (i or ii):
      i. Inadequate response or contraindication to acute vasodilator testing;
      ii. Trial and failure of, or contraindication to, at least one calcium channel blocker;
   b. WHO/NYHA Functional Class II, III or IV (Appendix C);
3. If Tyvaso is requested, prescribed dose does not exceed 9 breaths per treatment session (54 mcg of treprostinil) four times daily to be used with the Tyvasco Inhalation System (a second back-up system device is recommended).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. If Tyvaso is requested, prescribed dose does not exceed 9 breaths per treatment session (54 mcg of treprostinil) four times daily to be used with the Tyvasco Inhalation System (a second back-up system device is recommended).

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy;
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Treprostinil is a prostacyclin analogue. The major pharmacologic actions of treprostinil are direct vasodilation of pulmonary and systemic arterial vascular beds, inhibition of platelet aggregation, and inhibition of smooth muscle cell proliferation.

Formulations:

Inhalation solution

Tyvaso: 0.6 mg/mL (2.9 mL)
Tyvaso Refill: 0.6 mg/mL (2.9 mL)
Tyvaso Starter: 0.6 mg/mL (2.9 mL)

Injectable solution:

Remodulin: 1 mg/mL (20 mL); 2.5 mg/mL (20 mL); 5 mg/mL (20 mL); 10 mg/mL (20 mL)

Extended-release oral tablet:

Orenitram: 0.125 mg, 0.25 mg, 1 mg, 2.5 mg

FDA Approved Indications:

Orenitram is a prostacyclin vasodilator/extended-release oral tablet formulation indicated for:

- Treatment of PAH (WHO Group 1) to improve exercise capacity.
  - The study that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue disease. When used as the sole vasodilator, the effect of Orenitram on exercise is about 10% of the deficit, and the effect, if any, on a background of another vasodilator is probably less than this.

Remodulin is a prostacyclin vasodilator/subcutaneous or intravenous* injectable formulation indicated for:

- Treatment of PAH (WHO Group 1) to diminish symptoms associated with exercise.
  - Studies establishing effectiveness included patients with 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.

**It may be administered as a continuous subcutaneous infusion or continuous intravenous (IV) infusion; however, because of the risks associated with chronic indwelling central venous catheters, including serious blood stream infections (BSIs), reserve continuous intravenous infusion for patients who are intolerant of the subcutaneous route, or in whom these risks are considered warranted.*

- Patients with PAH requiring transition from Flolan (epoprostenol sodium) - Remodulin is indicated to diminish the rate of clinical deterioration. Consider the risks and benefits of each drug prior to transition.

Tyvaso is a prostacyclin vasodilator/inhalation solution* indicated for:

- Treatment of PAH (WHO Group 1) to improve exercise ability.

- Studies establishing effectiveness included predominately patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

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**The effects diminish over the minimum recommended dosing interval of 4 hours; treatment timing can be adjusted for planned activities. While there are long-term data on use of treprostinil by other routes of administration, 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). The controlled clinical experience was limited to 12 weeks in duration.*

Appendices

Appendix A: Abbreviation Key

- FC: functional classification
- NYHA: New York Heart Association
- PAH: pulmonary arterial hypertension
- PH: pulmonary hypertension
- WHO: World Health Organization

Appendix B: 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 C: 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 D**	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 D: 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) Tyvasco (inhalation)
			Iloprost	Ventavis (inhalation)
		Non-prostanoid prostacyclin receptor (IP receptor) agonist	Selexipag	Uptravi (oral tablet)
	Endothelin receptor antagonist	Selective receptor antagonist	Ambrisentan	Letairis (oral tablet)
		Nonselective dual action receptor antagonist	Bosentan	Tracleer (oral tablet)
			Macitentan	Opsummit (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	Riociguat	Adempas (oral tablet)

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
Policy split from CP.PHAR.33.PAH and converted to new template. Criteria: added specialist requirement; removed echocardiogram as an option for confirming a PH diagnosis; removed hard stop after 3 months of therapy. Appendices removed: 1) examples of calcium channel blocker contraindications; 2) nitrate therapy examples; 3) PAH definition.	02/16	03/16
FC II is added to the prostanoid class of PH drugs. Safety criteria were removed unless they 1) represent contraindications or black box warnings not covered by a REMS program, and 2) provide specific lab/imaging	02/17	03/17

Reviews, Revisions, and Approvals	Date	Approval Date
parameters that must be met prior to initiation of therapy. An efficacy statement is added to the continuation criteria. Initial and continuation durations increased to 6 and 12 months respectively. Appendices covering PH group, functional class and therapy reorganized.		

References

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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. The Health Plan 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. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.