

Clinical Policy: Bosentan (Tracleer)

Reference Number: CP.PHAR.191

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 bosentan (Tracleer®).

Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation® that Tracleer is **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. Prescribed dose of Tracleer does not exceed 125 mg twice daily.

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. Prescribed dose of Tracleer does not exceed 125 mg twice daily.

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; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Bosentan**Background***Description/Mechanism of Action:*

Tracleer (bosentan) is an endothelin receptor antagonist that belongs to a class of highly substituted pyrimidine derivatives, with no chiral centers. Bosentan is a specific and competitive antagonist at endothelin receptor types ET_A and ET_B. Bosentan has a slightly higher affinity for ET_A receptors than for ET_B receptors. The clinical impact of dual endothelin blockage is unknown. Endothelin-1 (ET-1) is a neurohormone, the effects of which are mediated by binding to ET_A and ET_B receptors in the endothelium and vascular smooth muscle. ET-1 concentrations are elevated in plasma and lung tissue of patients with pulmonary arterial hypertension, suggesting a pathogenic role for ET-1 in this disease.

Formulations:

Tracleer oral tablets: 62.5 mg, 125 mg

FDA Approved Indications:

Tracleer is an endothelin receptor antagonist/oral tablet formulation indicated for:

- Treatment of PAH (WHO Group 1) to improve exercise ability and to decrease clinical worsening.
 - Studies establishing effectiveness included predominantly patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH, PAH associated with connective tissue diseases, and PAH associated with congenital heart disease with left-to-right shunts.
 - Considerations for use: Patients with WHO Class II symptoms showed reduction in the rate of clinical deterioration and a trend for improvement in walk distance. Physicians should consider whether these benefits are sufficient to offset the risk of hepatotoxicity in WHO Class II patients, which may preclude future use as their disease progresses.

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 <i>*Member of the prostanoid class of fatty acid derivatives.</i>	Prostacyclin	Epoprostenol	Velettri (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	Upravi (oral tablet)
	Endothelin receptor antagonist (ETRA)		Selective receptor antagonist	Ambrisentan
		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 (sGC)	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
N/A	

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, updated contraindications based on PI. 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 represent contraindications or black box warnings not covered by a REMS program, and provide specific lab/imaging 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.	02/17	03/17

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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.

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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.

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