

Clinical Policy: Bosentan (Tracleer)

Reference Number: CP.PHAR.191

Effective Date: 03.16

Last Review Date: 02.18

Line of Business: Health Insurance Marketplace, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Bosentan (Tracleer[®]) is an endothelin receptor antagonist.

FDA Approved Indication(s)

Tracleer is indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability and to decrease clinical worsening.

Studies establishing effectiveness included predominantly patients with New York Heart Association (NYHA) Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital heart disease with left-to-right shunts (18%).

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.

Policy/Criteria

Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval 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. Diagnosis of PAH;
2. Prescribed by or in consultation with a cardiologist or pulmonologist;
3. Failure of a trial 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 a calcium channel blocker are experienced;
4. Dose does not exceed 125 mg twice daily.

Approval duration: 6 months

B. Other diagnoses/indications

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1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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 request is for a dose increase, new dose 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.
Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace, and CP.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 – HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.**

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FC: functional class	PAH: pulmonary arterial hypertension
FDA: Food and Drug Administration	PH: pulmonary hypertension
NYHA: New York Heart Association	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 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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: 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 D: 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 E**	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 E: 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	Prostacyclin	Epoprostenol	Velettri (IV) Flolan (IV) Flolan generic (IV)	
		*Member of the prostanoid class of fatty acid derivatives.	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 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

Indication	Dosing Regimen	Maximum Dose
Pulmonary arterial hypertension	Initially 62.5 mg PO BID for 4 weeks, then increased to 125 mg PO BID	250 mg/day

VI. Product Availability

Tablets: 62.5 mg, 125 mg

VII. References

1. Tracleer Prescribing Information. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; October 2016. Available at http://www.tracleer.com/assets/PDFs/Tracleer_Full_Prescribing_Information.pdf. Accessed November 20, 2017.

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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. Taichman D, Ornelas J, Chung L, et. al. CHEST guideline and expert panel report: Pharmacologic therapy for pulmonary arterial hypertension in adults. *Chest.* 2014; 146 (2): 449-475.
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, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Kardiol Pol.* 2015;73(12):1127-206. doi: 10.5603/KP.2015.0242

Reviews, Revisions, and Approvals	Date	P&T 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
1Q18 Annual Review: Combined with HIM.PA.SP5. Converted to new template. Removed WHO/NYHA classifications from initial criteria. References reviewed and updated.	11.20.17	02.18

Important Reminder

CLINICAL POLICY**Bosentan**

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.

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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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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