

Clinical Policy: Bosentan (Tracleer)

Reference Number: ERX.SPA.32

Effective Date: 07.01.16

Last Review Date: 02.22

Line of Business: Commercial, 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):

- In adults 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%).
- In pediatric patients aged 3 years and older with idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR), which is expected to result in an improvement in exercise ability

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] that bosentan 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 Tracleer, member must use generic bosentan, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 250 mg (4 tablets) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Pulmonary Arterial Hypertension (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

2. Member is responding positively to therapy;
3. If request is for brand Tracleer, member must use generic bosentan, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed 250 mg (4 tablets) per day.

Approval duration: 12 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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

PAH: pulmonary arterial hypertension

PH: pulmonary 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 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):
 - Pregnancy
 - Use with cyclosporine
 - Use with glyburide
 - Hypersensitivity
- Boxed warning(s):
 - Risk of hepatotoxicity (REMS program)
 - Embryo-fetal toxicity (REMS program)

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 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, and 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	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)
	Endothelin receptor antagonist	Non-prostanoid prostacyclin receptor (IP receptor) agonist	Selexipag	Upravi (oral tablet)	
			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 (PDE-5) inhibitor	Sildenafil	Revatio (IV, oral tablet, oral suspension)	
			Tadalafil	Adcirca (oral tablet)	
		Guanylate cyclase stimulant	Riociguat	Adempas (oral tablet)	

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PAH	Adults: Initially 62.5 mg PO BID for 4 weeks, then increased to 125 mg PO BID	250 mg/day

Indication	Dosing Regimen			Maximum Dose
	Pediatric patients:			
	Patient's age and weight	Initial 4 weeks	Maintenance (after 4 weeks)	
	> 12 years and > 40 kg	62.5 mg PO BID	125 mg PO BID	
	> 12 years and < 40 kg	62.5 mg PO BID	62.5 mg PO BID	
	≤ 12 years and ≥ 4 to 8 kg	16 mg PO BID	16 mg PO BID	
	≤ 12 years and > 8 to 16 kg	32 mg PO BID	32 mg PO BID	
	≤ 12 years and > 16 to 24 kg	48 mg PO BID	48 mg PO BID	
	≤ 12 years and > 24 to 40 kg	64 mg PO BID	64 mg PO BID	

VI. Product Availability

- Tablets: 62.5 mg, 125 mg
- Dispersible tablet for oral suspension: 32 mg

VII. References

1. Tracleer Prescribing Information. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; May 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021290s039.209279s005lbl.pdf. Accessed November 9, 2021.
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. doi: <https://doi.org/10.1016/j.chest.2018.11.030>.
4. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: Guidelines from the American Heart Association and American Thoracic Society. *Circulation.* 2015; 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. Yaghi S, Novikov A, Trandafirescu T. Clinical update on pulmonary hypertension. *J Investig Med.* 2020;0:1-7. doi:10.1136/jim-2020-001291.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Converted to new template. Removed WHO/NYHA classification from initial criteria. References reviewed and updated.	11.20.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	11.20.18	02.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: no significant changes; added max quantity per day; references reviewed and updated.	11.26.19	02.20
1Q 2021 annual review: for brand Tracleer requests, added requirement for medical justification why generic cannot be used; references reviewed and updated.	10.12.20	02.21
1Q 2022 annual review: no significant changes; revised medical justification language to “must use” language for generic redirection; added generic redirection to continued therapy; references reviewed and updated.	11.09.21	02.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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 policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2016 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.