BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.40.018

Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Cardiovascular Agents	**Original Policy Date:**	June 9, 2011
Subject:	Tracleer	**Page:**	1 of 8

Last Review Date: March 6, 2026

Tracleer

Description

Tracleer (bosentan)

Background
Pulmonary arterial hypertension is a rare disorder of the pulmonary arteries in which the pulmonary arterial pressure rises above normal levels in the absence of left ventricular failure. This condition can progress to cause right-sided heart failure and death (1-2). Tracleer is indicated for treatment of pulmonary arterial hypertension (PAH) which is classified by WHO as Group 1. Tracleer is used to treat pulmonary arterial hypertension (PAH, high blood pressure in the lungs) to improve exercise ability (1).

The World Health Organization (WHO) has classified pulmonary hypertension into five different groups: (2)

WHO Group 1: Pulmonary Arterial Hypertension (PAH)
1.1 Idiopathic (IPAH)
1.2 Heritable PAH
- 1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
- 1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
- 1.2.3 Unknown

1.3 Drug-and toxin-induced
1.4 Associated with:
- 1.4.1 Connective tissue diseases

1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart diseases (e.g. pulmonary artresia)
1.4.5 Schistosomiasis

1'. Pulmonary vena-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)

1''. Persistent pulmonary hypertension of the newborn (PPHN)

The diagnosis of WHO Group 1 PAH requires a right heart catheterization to demonstrate an mPAP ≥ 20mmHg at rest and a pulmonary vascular resistance (PVR) ≥ 3 Wood units, mean pulmonary capillary wedge pressure ≤ 15mmHg (to exclude pulmonary hypertension due to left heart disease, i.e. WHO Group 2 pulmonary hypertension) (5-7).

WHO Group 2: Pulmonary Hypertension Owing to Left Heart Disease

2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3: Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia

3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4: Chronic Thromboembolic Pulmonary Hypertension <CTEPHI

WHO Group 5: Pulmonary Hypertension with Unclear Multifactorial Mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher's disease, thyroid disorders

5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

The American College of Chest Physicians (ACCP) has published an updated clinical practice guideline for treating PAH. These guidelines use the New York Heart Association (NYHA) functional classification of physical activity scale to classify PAH patients in classes I-IV based on the severity of their symptoms. Tracleer is indicated for patients with NYHA Functional Class II, III or IV (2).

NYHA CLASSIFICATION OF ADULTS

Class I	Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.
Class II	Patients with pulmonary hypertension resulting in slight limitation of physical activity. These patients are comfortable at rest, but ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class III	Patients with pulmonary hypertension resulting in marked limitation of physical activity. These patients are comfortable at rest, but less than ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class IV	Patients with pulmonary hypertension resulting in inability to perform any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may be present at rest, and discomfort is increased by any physical activity.

(3)

Regulatory status

FDA-approved indications: Tracleer is an endothelin receptor antagonist indicated for the treatment of pulmonary arterial hypertension (WHO Group I): (1)

1. In adults 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 (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital heart disease with left-to-right shunts (18%)
2. 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

Tracleer has boxed warnings regarding risks of hepatotoxicity and embryo-fetal toxicity. Liver aminotransferase levels must be measured prior to initiation of treatment and then monthly and therapy adjusted accordingly. Discontinue Tracleer if liver aminotransferase elevations are

accompanied by clinical symptoms of hepatotoxicity (such as nausea, vomiting, fever, abdominal pain, jaundice, or unusual lethargy or fatigue) or increases in bilirubin. Females of reproductive potential must have pregnancy excluded prior and during treatment. To prevent pregnancy, females of reproductive potential must use two reliable forms of contraception during treatment and for one month after stopping Tracleer (1).

Co-administration with cyclosporine A is contraindicated due to the markedly increased plasma concentrations of Tracleer. An increased risk of elevated liver aminotransferases was observed in patients receiving concomitant therapy with glyburide. Therefore, the concomitant administration of Tracleer and glyburide is contraindicated, and alternative hypoglycemic agents should be considered (1).

Should signs of pulmonary edema occur, consider the possibility of associated pulmonary veno-occlusive disease and consider whether Tracleer should be discontinued. Treatment with Tracleer can cause a dose-related decrease in hemoglobin and hematocrit. There have been postmarketing reports of decreases in hemoglobin concentration and hematocrit that have resulted in anemia requiring transfusion. It is recommended that hemoglobin concentrations be checked after 1 and 3 months, and every 3 months thereafter (1).

Due to the serious side effects associated with Tracleer, the FDA requires the manufacturer to provide a Risk Evaluation and Mitigation Strategy (REMS) program in which the patient, physician, and pharmacy must enroll and meet criteria for the prescribing, dispensing, and administration of the drug (1).

Related policies
Adcirca, Adempas, Flolan/Veletri, Letairis, Opsumit, Opsynvi, Orenitram, PDE5 Inhibitor powders, Remodulin, Revatio, Tyvaso, Uptravi, Ventavis, Winrevair

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Tracleer may be considered **medically necessary** if the conditions indicated below are met.

Tracleer may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

1. Pulmonary Arterial Hypertension (PAH) – **WHO Group I**
   a. Prescribed by or recommended by a cardiologist or pulmonologist
   b. Patient and prescriber enrolled in and meet all the conditions of the bosentan REMS Program
   c. **Brand Tracleer 62.5mg and 125mg ONLY**: Inadequate treatment response, intolerance, or contraindication to generic Tracleer: bosentan

AND ALL of the following for patients 18 years of age or older:

1. NYHA functional classification of physical activity - Class II, III, or IV
2. **NOT** receiving treatment with cyclosporine A or glyburide (Diabeta, Micronase, Glynase or Glucovance)
3. Female patients of reproductive potential **ONLY**: pregnancy will be excluded before and during treatment with Tracleer, and patient will be advised to use two reliable forms of contraception during treatment and for one month after stopping Tracleer
4. Prescriber agrees to monitor for pulmonary edema and discontinue if confirmed

Prior – Approval *Renewal* Requirements

Diagnosis

Patient must have the following:

1. Pulmonary Arterial Hypertension (PAH) – **WHO Group I**
   a. Prescribed by or recommended by a cardiologist or pulmonologist
   b. Patient and prescriber enrolled in and meet all the conditions of the bosentan REMS Program
   c. **Brand Tracleer 62.5mg and 125mg ONLY**: Inadequate treatment response, intolerance, or contraindication to generic Tracleer: bosentan

AND ALL of the following for patients 18 years of age or older:

1. Symptoms have improved or stabilized

2. **NOT** receiving treatment with cyclosporine A or glyburide (Diabeta, Micronase, Glynase or Glucovance)
3. Female patients of reproductive potential **ONLY**: pregnancy will be excluded during treatment with Tracleer, and patient will be advised to use two reliable forms of contraception during treatment and for one month after stopping Tracleer
4. Prescriber agrees to monitor for pulmonary edema and discontinue if confirmed

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 2 years

Prior – Approval *Renewal* Limits
Same as above

Rationale

Summary

Pulmonary arterial hypertension is a rare disorder of the pulmonary arteries in which the pulmonary arterial pressure rises above normal levels in the absence of left ventricular failure. This condition can progress to cause right-sided heart failure and death (1,2). Tracleer is a endothelin receptor antagonist indicated for treatment of pulmonary arterial hypertension (WHO Group I) in patients with NYHA class II, III, or IV to improve exercise ability and to decrease clinical worsening. Due to the serious side effects associated with Tracleer, the FDA requires the manufacturer to provide a Risk Evaluation and Mitigation Strategy (REMS) program in which the patient, physician, and pharmacy must enroll and meet criteria for the prescribing, dispensing, and administration of the drug (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Tracleer while maintaining optimal therapeutic outcomes.

References

1. Tracleer [package insert]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.; November 2025.
2. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll* Cardiol. 2013; 62:034-841.
3. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest.* 2014; 46(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; 132(21): 2037-99.
5. Simonneau G, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53(1) Epub 2019 Jan 24.
6. Rose-Jones LJ and Mclaughlin V. Pulmonary Hypertension: Types and Treatments. Curr Cardiol Rev. 2015 Feb; 11(1): 73–79.
7. Rudolf KF, et al. Usefulness of pulmonary capillary wedge pressure as a correlate of left ventricular filling pressures in pulmonary arterial hypertension. The Journal of Heart and Lung Transplantation, Vol33, No2. February 2014.

Policy History

Date	Action	Reason
June 2012	Annual editorial and reference update	
March 2013	Annual editorial and reference update	
March 2014	Annual review	
March 2015	Annual editorial and reference update	
June 2016	Annual editorial review and reference update Addition of age 18 and the prescriber agrees to monitor for pulmonary edema and discontinue if confirmed Policy number change from 5.06.07 to 5.40.18	
September 2017	Annual editorial review and reference update	
November 2017	Change in age of approval from 18 years of age and older to no age restrictions	
March 2018	Annual review	
September 2019	Annual editorial review and reference update. Changed approval duration from lifetime to 2 years	
March 2020	Annual review. Revised background section and added initial requirement of prescribed by or recommended by a cardiologist or pulmonologist per SME	

December 2021	Annual review and reference update. Added requirement that brand Tracleer 62.5mg and 125mg have to t/f the preferred product bosentan. Updated REMS program and female contraception requirements to align with current PI.
September 2022	Annual review and reference update
December 2022	Annual review
September 2023	Annual review and reference update
March 2024	Annual review
September 2024	Annual review and reference update
March 2025	Annual review
December 2025	Annual review. Removed MedEx requirement and switched to t/f
March 2026	Annual editorial review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.