

PHARMACY POLICY STATEMENT

North Carolina Marketplace

DRUG NAME	Endothelin Receptor Antagonists for Pulmonary Arterial Hypertension: Letairis (ambrisentan), Opsumit (macitentan), Tracleer (bosentan)
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Pulmonary Arterial Hypertension is a rare but serious condition characterized by elevated pulmonary arterial resistance. Letairis, Opsumit and Tracleer are endothelin receptor antagonists approved for the treatment of pulmonary arterial hypertension (PAH) World Health Organization (WHO) Group 1. Letairis is indicated to improve exercise ability and delay clinical worsening in PAH. It can also be used in combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability. Opsumit is indicated for the treatment of PAH to reduce the risks of disease progression and hospitalization. Tracleer is indicated in adults to improve exercise ability and to decrease clinical worsening for PAH. It can also be used in pediatric patients with idiopathic or congenital PAH to improve pulmonary vascular resistance.

Endothelin Receptor Antagonists will be considered for coverage when the following criteria are met:

Pulmonary Arterial Hypertension [WHO Group 1]

For **initial** authorization:

1. For Tracleer, member is at least 3 years of age or older; AND
2. For Letairis and Opsumit, member is at least 18 years of age or older; AND
3. For Opsumit, member has had a trial and failure of generic ambrisentan or bosentan; AND
4. Medication must be prescribed by or in consultation with a cardiologist or pulmonologist; AND
5. Member must have a diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH) confirmed by right heart catheterization; AND
6. Member has documentation of WHO functional class II, III or IV; AND
7. Member must have documentation of **ONE** of the following:
 - a) Patient had an acute response to vasodilator testing AND has tried a calcium channel blocker (CCB) for at least 3 months;
 - b) Patient did not have a response to vasodilator testing;
 - c) Patient cannot undergo vasodilator testing;
 - d) Patient cannot take CCB therapy.
8. **Dosage allowed/Quantity limit:**
 - Opsumit: 10 mg once daily. Quantity Limit: 30 tablets per 30 days.
 - Letairis: Initiate at 5 mg once daily. May increase to 10 mg once daily. Quantity Limit: 30 tablets per 30 days.
 - Tracleer: Quantity Limit: 120 tablets per 30 days.
 - a) Patients 12 years and older:
 - a. > 40kg: 62.5 mg PO BID for 4 weeks, then increased to 125 mg PO BID
 - b. < 40 kg: 62.5 mg PO BID
 - b) Patients 12 years and younger:
 - a. ≥ 4-8 kg: 16 mg twice daily

- b. > 8-16 kg: 32 mg twice daily
- c. > 16-24 kg: 48 mg twice daily
- d. > 24-40 kg: 64 mg twice daily

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Member has documentation of improvement in signs and symptoms of disease as evidenced by at least **ONE** of the following:
 - a) Stabilization or improvement in WHO functional class (see appendix);
 - b) Stabilization or improvement in 6MWD (6-minute walk distance);
 - c) Reduction in PAH-related hospitalizations.

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Endothelin Receptor Antagonists not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
06/15/2011	Pulmonary Arterial Hypertension policy creation.
05/13/2014	Combined all PAH agents into one policy
07/09/2015	Revised guidelines for therapy aligning with CMS
08/18/2015	Revised guidelines to include diagnosis criteria
10/13/2021	Separated PAH agents by drug class; Updated guidelines; Added provider specialty
04/24/2023	Updated guidelines. Added quantity limits. Updated dosing for Tracleer.
04/19/2024	Added trial of generic ambrisentan or bosentan for Opsumit
04/30/2024	Updated/added references; removed PAH diagnosis from appendix; added functional class requirement

Appendix:

World Health Organization Functional Assessment Classification	
Class I	Patients without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea, fatigue, chest pain or near syncope.
Class II	Patients with slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity increases dyspnea, fatigue, chest pain, or near syncope.
Class III	Patients with marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity increases dyspnea, fatigue, chest pain, or near syncope.
Class IV	Patients unable to carry out any physical activity without symptoms. These patients may have signs of right-heart failure. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

References:

1. Letairis [package insert]. Foster City, CA: Gilead Sciences, Inc; 2019.
2. Opsumit [package insert]. San Francisco, CA: Actelion Pharmaceuticals US, Inc.; 2024.
3. Tracleer [package insert]. San Francisco, CA: Actelion Pharmaceuticals US, Inc.; 2024.
4. Coons JC, Pogue K, Kolodziej AR, Hirsch GA, George MP. Pulmonary Arterial Hypertension: a Pharmacotherapeutic Update. *Curr Cardiol Rep*. 2019;21(11):141. Published 2019 Nov 22. doi:10.1007/s11886-019-1235-4
5. Klingler JR, Elliott CG, Levine DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guideline and Expert Panel Report [published correction appears in *Chest*. 2021 Jan;159(1):457]. *Chest*. 2019;155(3):565-586. doi:10.1016/j.chest.2018.11.030
6. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J*. 2023;61(1):2200879. Published 2023 Jan 6. doi:10.1183/13993003.00879-2022
7. Abman SH, Hansmann G, Archer SL, et al. Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic Society [published correction appears in *Circulation*. 2016 Jan 26;133(4):e368]. *Circulation*. 2015;132(21):2037-2099. doi:10.1161/CIR.0000000000000329

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