Pulmonary Arterial Hypertension: Endothelin Receptor Antagonists Utilization Management Criteria

Therapeutic Class:	Pulmonary Arterial Hypertension: Endothelin Receptor Antagonists
Non-Preferred Agents:	Bosentan, Letairis (ambrisentan), Opsumit (macitentan), Opsynvi (macitentan and tadalafil), Tracleer (bosentan) tablet for suspension
Preferred Agents:	Ambrisentan generic, Tracleer (bosentan) 62.5 mg, 125 mg tablet
Implementation Date:	1/1/2026
Prepared For:	CT
PDL Status:	Non-preferred
Purpose:	Pulmonary hypertension (PH) is a disease characterized by elevated pulmonary artery pressure. The World Health Organization (WHO) classifies patients with PH into five groups: Group 1 (pulmonary arterial hypertension [PAH]), Group 2 (PH due to left heart disease), Group 3 (PH due to chronic lung disease and/or hypoxemia), Group 4 (PH due to pulmonary artery obstructions), Group 5 (PH due to unclear mechanisms). PAH is a progressive disease characterized by dyspnea, fatigue, syncope, and edema. Patients with PAH are typically evaluated for baseline risk of disease progression and death prior to the selection of therapy; risk stratification determines initial treatment regimen selection. PAH-specific agents include prostacyclin pathway agents, endothelin-1 receptor antagonists, phosphodiesterase-5 inhibitors, a soluble guanylyl cyclase stimulator, an activin-signaling inhibitor, or, more rarely used, calcium channel blockers. The oral endothelin receptor antagonists, ambrisentan, bosentan, and macitentan, are competitive antagonists at receptor subtypes endothelin $(ET)_A$ and ET_B. These agents have different affinities for each receptor subtype. Both ET_A and ET_B receptors mediate the effects of ET-1 (potent autocrine and paracrine peptide) in the vascular smooth muscle and endothelium. The predominant actions of ET_A are vasoconstriction and cell proliferation; in contrast, the predominant actions of ET_B are ET-1 clearance, antiproliferation, and vasodilation. All three endothelin receptor antagonist agents are approved for treating World Health Organization (WHO) Group 1 PAH. Bosentan is only available through a restricted Risk Evaluation and Mitigation Strategy (REMS) program due to the risk of hepatotoxicity. In April of 2025, the FDA determined that REMS programs were no longer necessary for ambrisentan and macitentan. Both agents remain contraindicated in pregnancy.

Table 1. Pulmonary Arterial Hypertension: Endothelin Receptor Antagonists

Generic Name	Brand Name	Approved Indications	Route of Administration	Generic Availability
Ambrisentan	Letairis®	PAH (WHO group 1)	Oral	Y
Bosentan	Tracleer®	PAH (WHO group 1)	Oral	Y
Macitentan	Opsumit®	PAH (WHO group 1)	Oral	N
Macitentan/tadalafil	Opsynvi®	PAH (WHO group 1)	Oral	N

Abbreviations: Abbreviations: PAH, pulmonary arterial hypertension; WHO, World Health Organization.

All authorizations must be prescribed in accordance with FDA approved labeling. Use of samples to initiate therapy does not meet step therapy and/or continuation of therapy prior authorization requirements. Prior therapies will be verified through pharmacy claims and/or submitted chart notes.

General Approval Criteria:

- Requested quantity in accordance with FDA approved product labelling
- For specific formulation requests
  - **For brand requests when a therapeutically equivalent generic is preferred:** Provider must provide a documented medical reason the preferred generic formulation cannot be used
  - **For generic requests when a therapeutically equivalent brand is preferred:** Provider must provide a documented medical reason the preferred brand formulation cannot be used
  - **For non-preferred dosage or formulation requests:** Provider must provide a documented medical reason the preferred dosage or formulation cannot be used

Initial Therapy – All the following must be met:

- Provider has expertise in treating patients with pulmonary hypertension
- Documented diagnosis of pulmonary hypertension
- Claim is for a preferred agent **OR**
- Failure to achieve desired therapeutic outcomes with a trial of **ONE** preferred agent (defined as 30 day trial) **OR** documentation of adverse drug event/adverse drug reaction or contraindication

Additional Criteria For Opsynvi

- Quantity limit: 1 tablet per day

For Tracleer Tablet for Suspension

- Documentation of medical reason why a preferred formulation cannot be used. *(Trial and failure of preferred dosage form is not required for patients unable to swallow solid dosage forms)*
- Provider attests to having met the REMS requirements for counseling and monitoring

Initial PA length: 1 year

Exclusion Criteria: Therapy will deny for the following

- Approval criteria not met
- Patient is pregnant

Continuation Therapy: Documented compliance on current therapy **AND** Documented continued clinical benefit **AND**

- For specific formulation requests
    - **For brand requests when a therapeutically equivalent generic is preferred:** Provider must provide a documented medical reason the preferred generic formulation cannot be used
    - **For generic requests when a therapeutically equivalent brand is preferred:** Provider must provide a documented medical reason the preferred brand formulation cannot be used
    - **For non-preferred dosage or formulation requests:** Provider must provide a documented medical reason the preferred dosage or formulation cannot be used

Continuation Length: 1 year

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Revision History

Date	Version	Revisions
11/7/2025	V1	Document approved by DSS

