MEDICAL MUTUAL®

Drug Policy

Policy:	**Endothelin Receptor Antagonists (ERAs)** **Tracleer (bosentan)** **Letairis (ambrisentan)** **Opsumit (macitentan)** **Opsynvi (macitentan/tadalafil)**	**Annual Review Date:** **02/20/2025** **Last Revised Date:** **02/20/2025**

OVERVIEW

Letairis, Opsumit, and Tracleer are oral endothelin receptor antagonists indicated for the treatment of **pulmonary arterial hypertension** (PAH) **World Health Organization (WHO) Group 1**.[1-3] Of note, Letairis and Tracleer tablets (traditional, not tablets for oral suspension) are available as generics.

- Letairis is indicated to improve exercise ability and delay clinical worsening as well as for use in combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.[2]
- Opsumit is noted to reduce the risks of disease progression and hospitalization for PAH.[3]
- Tracleer is indicated in adults to improve exercise ability and decrease the rate of clinical worsening and in pediatric patients ≥ 3 years of age with idiopathic or congenital PAH to improve pulmonary vascular resistance, which is expected to result in an improvement in exercise ability.[1]

POLICY STATEMENT

This policy involves the use of ERAs. Prior authorization is recommended for pharmacy benefit coverage of ERAs. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with ERAs as well as the monitoring required for adverse events and long-term efficacy, initial approval requires ERAs be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of ERAs is recommended in those who meet the following criteria:

1. <u>Pulmonary Arterial Hypertension (World Health Organization [WHO] Group 1), Initial Therapy</u>

Approve for the duration noted if the patient meets ONE of the following (A <u>or</u> B):

A) <u>Initial Therapy</u>. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, <u>and</u> iv).

i. Patient has a diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH); AND

ii. Patient meets BOTH of the following (a and b):
  a) Patient has had a right heart catheterization*; AND
  b) Results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
iii. The agent is prescribed by or in consultation with a cardiologist or pulmonologist; AND
iv. If the request is for brand Letairis or Tracleer, the patient has failed a trial of the respective generic product and/or the patient cannot take the respective generic product due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the brand and the generic product which would result in a significant allergy or serious adverse reaction per the prescribing physician*.

B) Patient is Currently Receiving the Requested Endothelin Receptor Antagonist (i.e., ambrisentan [Letairis, generic], Opsumit, or bosentan [Tracleer, generic]) or Opsynvi. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, iv, and v):
i. Patient has a diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH); AND
ii. Patient meets BOTH of the following (a and b):
  a) Patient has had a right heart catheterization*; AND
  Note: This refers to prior to starting therapy with a medication for WHO Group 1 PAH
  b) Results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
iii. The medication is prescribed by or in consultation with a cardiologist or a pulmonologist; AND
iv. The patient is currently experiencing a beneficial response as determined by the physician (e.g. improvement in functional class or quality of life, or in other hemodynamic or clinical parameters); AND
v. If the request is for brand Letairis or Tracleer, the patient has failed a trial of the respective generic product and/or the patient cannot take the respective generic product due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the brand and the bioequivalent generic product which would result in a significant allergy or serious adverse reaction per the prescribing physician*.

2. Chronic Thromboembolic Pulmonary Hypertension (CTEPH), WHO Group 4
Criteria. *Patient must meet the following criteria*

A. The request is for bosentan (Tracleer, generic); AND
B. The medication is prescribed by or in consultation with a cardiologist or pulmonologist; AND
C. The patient meets ONE of the following (i, ii, or iii):
  i. Patient has tried Adempas; OR
  ii. According to the prescriber, use of Adempas is contraindicated; OR
  Note: Examples of contraindications to use of Adempas include that the patient is receiving nitrates or nitric oxide donors, the patient is receiving a phosphodiesterase inhibitor such as sildenafil or tadalafil, or that the patient is hypotensive or is at risk for hypotension.
  iii. Patient is currently receiving bosentan; AND
D. The patient has been treated surgically or CTEPH is inoperable
E. For brand Tracleer, the patient has failed a trial of generic bosentan and/or the patient cannot take generic bosentan due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the brand and the bioequivalent generic product which would result in a significant allergy or serious adverse reaction per the prescribing physician*.

3. **Digital Ulcers in Systemic Sclerosis**
Criteria. *Patient must meet the following criteria*

A. The request is for bosentan (Tracleer, generic); AND
B. The patient meets one of the following:
  a. The patient has tried one vasodilator/prostanoid therapy [examples include epoprostenol injection and alprostadil injection]; OR
  b. The patient has tried two other therapies for this condition such as calcium channel blockers (CCBs) [examples include amlodipine, felodipine, and nifedipine], phosphodiesterase type 5 (PDE5) inhibitors [examples include sildenafil and Levitra (vardenafil)], alpha-adrenergic blockers [example: prazosin], nitroglycerin, or angiotensin converting enzyme (ACE) inhibitors; AND
C. For brand Tracleer, the patient has failed a trial of generic bosentan and/or the patient cannot take generic bosentan due to a formulation difference in the inactive ingredient(s) [e.g. differences in dyes, fillers, preservatives] between the brand and the bioequivalent generic product which would result in a significant allergy or serious adverse reaction per the prescribing physician*.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

ERAs have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Concurrent Use of Opsynvi with Guanylate Cyclase Stimulators.** Use of Opsynvi with guanylate cyclase stimulators is contraindicated. An example of a guanylate cyclase stimulator is Adempas (riociguat).

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

***Documentation Requirements:**
The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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