ENDOTHELIN RECEPTOR ANTAGONISTS

Generic	Brand	HICL	GCN	Exception/Other
BOSENTAN	TRACLEER	22990		
AMBRISENTAN	LETAIRIS	34849		
MACITENTAN	OPSUMIT	40677		

**** Please use the criteria for the specific drug requested ****

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

LETAIRIS

1. Does the patient have a diagnosis of pulmonary arterial hypertension (WHO Group 1) and meets **ALL** of the following criteria?
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - Documented confirmatory PAH diagnosis based on right heart catheterization with the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units
   - The patient has NYHA-WHO Functional Class II to IV symptoms
   - The patient does not have idiopathic pulmonary fibrosis (IPF)

   If yes, **approve Letairis for 12 months by HICL for #1 tablet per day**.
   If no, do not approve.
   DENIAL TEXT: The guideline named **ENDOTHELIN RECEPTOR ANTAGONISTS (Letairis)** requires a diagnosis of pulmonary arterial hypertension. The following criteria must also be met:
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - Documented confirmatory PAH diagnosis based on right heart catheterization with the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units
   - The patient has NYHA-WHO Functional Class II to IV symptoms
   - The patient does not have idiopathic pulmonary fibrosis (IPF)

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ENDOTHELIN RECEPTOR ANTAGONISTS

INITIAL CRITERIA (CONTINUED)

TRACLEER

1. Does the patient have a diagnosis of pulmonary arterial hypertension (WHO Group 1) and meets **ALL** of the following criteria?
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - The patient is 3 years of age or older
   - Documented confirmatory PAH diagnosis based on right heart catheterization with the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units
   - The patient has NYHA-WHO Functional Class II to IV symptoms
   - The patient does not have idiopathic pulmonary fibrosis (IPF)
   - The patient is not concurrently taking cyclosporine A or glyburide

   If yes, **approve Tracleer for 12 months by GPID for all the following strengths with the following quantity limits:**
   - **62.5mg tablet (GPID 14979): #2 tablets per day.**
   - **125mg tablet (GPID 14978): #2 tablets per day.**
   - **32mg tablet for suspension (GPID 43819): #4 tablets per day.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **ENDOTHELIN RECEPTOR ANTAGONISTS (Tracleer)** requires a diagnosis of pulmonary arterial hypertension. The following criteria must also be met.
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - The patient is 3 years of age or older
   - Documented confirmatory PAH diagnosis based on right heart catheterization with the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units
   - The patient has NYHA-WHO Functional Class II to IV symptoms
   - The patient does not have idiopathic pulmonary fibrosis (IPF)
   - The patient is not concurrently taking cyclosporine A or glyburide

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ENDOTHELIN RECEPTOR ANTAGONISTS

INITIAL CRITERIA (CONTINUED)

OPSUMIT

1. Does the patient have a diagnosis of pulmonary arterial hypertension (WHO Group 1) and meets **ALL** of the following criteria?
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - Documented confirmatory PAH diagnosis based on right heart catheterization with the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units
   - The patient has NYHA-WHO Functional Class II to IV symptoms

   If yes, **approve Opsumit for 12 months by HICL for #1 tablet per day.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **ENDOTHELIN RECEPTOR ANTAGONISTS (Opsumit)** requires a diagnosis of pulmonary arterial hypertension. The following criteria must also be met.
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - Documented confirmatory PAH diagnosis based on right heart catheterization with the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units
   - The patient has NYHA-WHO Functional Class II to IV symptoms

RENEWAL CRITERIA

1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1)?

   If yes, continue to #2
   If no, do not approve.
   DENIAL TEXT: See the renewal text at the end of the guideline.

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RENEWAL CRITERIA (CONTINUED)

2. Is the request for Tracleer and the patient is between the ages of 3 and 17 years old and meets one of the following criteria?
   - The patient has demonstrated an improvement in pulmonary vascular resistance (PVR) **OR**
   - The patient has remained stable or shown improvement in exercise ability (e.g., 6-minute walk test, World Health Organization [WHO] functional class symptoms)

   If yes, **approve Tracleer for 12 months by GPID for all the following strengths with the following quantity limits:**
   - **62.5mg tablet (GPID 14979): #2 tablets per day.**
   - **125mg tablet (GPID 14978): #2 tablets per day.**
   - **32mg tablet for suspension (GPID 43819): #4 tablets per day.**

   If no, continue to #3.

3. Has the patient shown improvement from baseline in the 6-minute walk distance test?

   If yes**, approve the requested agent for 12 months with the following quantity limits:**
   - **Letairis: approve by HICL for #1 per day.**
   - **Tracleer: approve by GPID for all the following strengths with the following quantity limits:**
     - **62.5mg tablet (GPID 14979): #2 tablets per day.**
     - **125mg tablet (GPID 14978): #2 tablets per day.**
     - **32mg tablet for suspension (GPID 43819): #4 tablets per day.**
   - **Opsumit: approve by HICL for #1 per day.**

   If no, continue to #4.

4. Has the patient remained stable from baseline in the 6-minute walk distance test?

   If yes continue to #5.
   If no, do not approve.
   DENIAL TEXT: See the renewal text at the end of the guideline.

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RENEWAL CRITERIA (CONTINUED)

5. Has the patient's WHO functional class remained stable or has improved?

   If yes, **approve the requested agent for 12 months with the following quantity limits:**
   - **Letairis: approve by HICL for #1 per day.**
   - **Tracleer: approve by GPID for all the following strengths with the following quantity limits:**
     - **62.5mg tablet (GPID 14979): #2 tablets per day.**
     - **125mg tablet (GPID 14978): #2 tablets per day.**
     - **32mg tablet for suspension (GPID 43819): #4 tablets per day.**
   - **Opsumit: approve by HICL for #1 per day.**

   If no, do not approve.
   DENIAL TEXT: See the renewal text at the end of the guideline.

RENEWAL DENIAL TEXT: The guideline named **ENDOTHELIN RECEPTOR ANTAGONISTS (Letairis, Tracleer, Opsumit)** requires a diagnosis of pulmonary arterial hypertension (PAH) and the following criteria must also be met for renewal:
- **For Tracleer patients 18 years of age or older, Letairis and Opsumit:** Patient shows improvement from baseline in the 6-minute walk distance **OR** that the patient has a stable 6-minute walk distance with a stable or improved Word Health Organization (WHO) functional class symptom.
- **For Tracleer patients age 3-17:** The patient has demonstrated an improvement in pulmonary vascular resistance (PVR) **OR** has remained stable or shown improvement in exercise ability (e.g. 6-minute walk test, World Health Organization [WHO] functional class symptoms).

RATIONALE
Ensure appropriate utilization of Tracleer, Letairis and Opsumit.

Diagnosis of PAH involves a logical sequence of steps utilizing different diagnostic tests to assist in confirmation of PAH (chest x-ray, echocardiogram, electrocardiogram, CT angiogram, pulmonary function tests, VQ scan); however, right heart catheterization (RHC) remains the gold standard and is an essential component in the definitive diagnosis, prognosis, and evaluation of PAH. RHC is critical in distinguishing PH due to other etiologies, for example PH due to left heart disease (eg. diastolic dysfunction) or severe lung disease, which may appear similar to PAH on an echocardiogram. In addition, RHC can be used to monitor the therapeutic and adverse effects of medical interventions, to assess the severity of hemodynamic impairment, and to test the vasoreactivity of the pulmonary circulation.

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ENDOTHELIN RECEPTOR ANTAGONISTS

FDA APPROVED INDICATIONS

LETAIRIS is an endothelin receptor antagonist indicated for the treatment of pulmonary arterial hypertension (WHO Group 1):

- in patients with NYHA-WHO class II or III symptoms to improve exercise capacity and delay clinical worsening. In addition, Letairis is approved in combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.

TRACLEER is an endothelin receptor antagonist indicated for the treatment of pulmonary arterial hypertension (WHO Group 1)

- in adults to improve exercise ability and to decrease clinical worsening. Studies establishing effectiveness included predominantly patients with WHO 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

OPSUMIT is an endothelin receptor antagonist indicated for the treatment of pulmonary arterial hypertension (WHO Group 1) to delay disease progression, including death, initiation of intravenous or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6 minute walk distance, worsened PAH symptoms and need for additional PAH treatment. Opsumit also reduced hospitalization for PAH.

REFERENCES

- Actelion Pharmaceuticals US, Inc. Tracleer package insert. South San Francisco, CA. September 2017.
- Actelion Pharmaceuticals US, Inc. Opsumit package insert. South San Francisco, CA. October 2013.
- Gilead Sciences, Inc., Letairis package insert. Foster City, CA. October 2015.
- Taichman DB, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults: CHEST guideline and expert panel report. CHEST 2014 Aug;146(2):449-75.
- N Galiè et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS) endorsed by: Assoication for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J 2015 Aug 29.
- Hoeper MM, et al. Definitions and diagnosis of pulmonary hypertension. J Am Coll Cardiol 2013;62(Suppl):D42-D50.

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Library	Commercial	NSA
Yes	Yes	No

Part D Effective: N/A
Commercial Effective: 12/08/17
Created: 09/05
Client Approval: 11/17
P&T Approval: 01/18