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

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

REMODULIN
1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) and meet ALL of the following criteria?
   - The patient has New York Heart Association-World Health Organization (NYHA-WHO) Functional Class III to IV symptoms
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - The patient had a previous trial of or contraindication to a phosphodiesterase-5 inhibitor (e.g., Adcirca or Revatio) OR an endothelin receptor antagonist (e.g., Tracleer, Letairis, Opsumit)
   - 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

If yes, **approve for 12 months by HICL.**
If no, do not approve.

DENIAL TEXT: The guideline named TREPROSTINIL (Remodulin) requires a diagnosis of pulmonary arterial hypertension. In addition, 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 unit

(Remodulin initial denial text continued on next page)

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TREPROSTINIL

INITIAL CRITERIA - REMODULIN (CONTINUED)

- The patient has NYHA-WHO Functional Class III to IV symptoms
- The patient had a previous trial of or contraindication to a phosphodiesterase-5 inhibitor (e.g., Adcirca or Revatio) or an endothelin receptor antagonist (e.g., Tracleer, Letairis, Opsumit)

TYVASO

1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) and meet 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 New York Heart Association-World Health Organization (NYHA-WHO) Functional Class III to IV symptoms

If yes, **approve for 12 months by HICL.**
If no, do not approve.

**DENIAL TEXT:** The guideline named TREPROSTINIL (Tyvaso) requires a diagnosis of pulmonary arterial hypertension. In addition, 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 III to IV symptoms

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ORENITRAM

1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) and meet 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 New York Heart Association-World Health Organization (NYHA-WHO) Functional Class II to IV symptoms
   - The patient does not have severe hepatic impairment
   - The patient has tried two preferred formulary alternatives including Uptravi and ONE of the following agents:
     - A phosphodiesterase-5 inhibitor (e.g., Adcirca or Revatio)
     - An endothelin receptor antagonist (e.g., Tracleer, Letairis, Opsumit)

If yes, approve for 12 months by HICL.
If no, do not approve.

DENIAL TEXT: The guideline named TREPROSTINIL (Orenitram) requires a diagnosis of pulmonary arterial hypertension. In addition, 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 severe hepatic impairment
   - The patient must have a previous trial of two preferred formulary alternatives, including Uptravi and ONE of the following agents:
     - A phosphodiesterase-5 inhibitor (e.g., Adcirca or Revatio)
     - An endothelin receptor antagonist (e.g., Tracleer, Letairis, Opsumit)
TREPROSTINIL

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) and meet ALL of the following criteria?
   - The patient has shown improvement or has remained stable from baseline in the 6-minute walk distance test
   - The patient’s World Health Organization (WHO) functional class has improved or remained stable

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

2. Is the request for Tyvaso or Orenitram?

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

3. Is the request for Remodulin and the patient has New York Heart Association-World Health Organization (NYHA-WHO) Functional Class II-IV symptoms?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   **DENIAL TEXT:** See the renewal denial text at the end of the guideline.

**RENEWAL DENIAL TEXT:** The guideline named TREPROSTINIL (Remodulin, Tyvaso, Orenitram) requires for renewal a diagnosis of pulmonary arterial hypertension. In addition, the following criteria must also be met:
- The patient has shown improvement or has remained stable from baseline in the 6-minute walk distance test
- The patient’s World Health Organization (WHO) functional class has improved or remained stable

**Requests for treprostinil (Remodulin)** also require that the patient has New York Heart Association-World Health Organization (NYHA-WHO) Functional Class II-IV symptoms

**RATIONALE**
Ensure appropriate use of Remodulin, Tyvaso and Orenitram.

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TREPROSTINIL

FDA APPROVED INDICATION
REMODULIN is indicated as a continuous subcutaneous infusion or intravenous infusion for the treatment of pulmonary arterial hypertension in patients with NYHA Class II-IV symptoms to diminish symptoms associated with exercise. Although injectable treprostinil is FDA-approved for use in functional class II patients, it would rarely be recommended for these patients due to its complex administration, cost, safety concerns and adverse effects. Thus, a trial of an oral Phosphodiesterase-5 inhibitor or an Endothelin receptor antagonist is required prior to approval for functional class II PAH.

TYVASO is indicated to increase walk distance in patients with WHO Group I pulmonary arterial hypertension and NYHA Class III symptoms.

ORENITRAM is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity. The study that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH (75%) or PAH associated with connective tissue disease (19%).

When used as the sole vasodilator, the effect of Orenitram on exercise is about 10% of the deficit, and the effect, if any, on a background of another vasodilator is probably less than this. Orenitram is probably most useful to replace subcutaneous, intravenous, or inhaled treprostinil, but this use has not been studied.

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 (e.g. 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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REFERENCES


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