PRIOR AUTHORIZATION POLICY

POLICY: Pulmonary Arterial Hypertension – Orenitram Prior Authorization Policy
- Orenitram® (treprostinil extended-release tablets – United Therapeutics)

REVIEW DATE: 10/09/2024

OVERVIEW

Orenitram, a prostacyclin mimetic, is indicated for the treatment of **pulmonary arterial hypertension (PAH) World Health Organization (WHO) Group 1** to delay disease progression and to improve exercise capacity.[1]

Disease Overview

PAH is a serious but rare condition impacting fewer than 20,000 patients in the US.[2,3] It is classified within Group 1 pulmonary hypertension among the five different groups that are recognized. In this progressive disorder, the small arteries in the lungs become narrowed, restricted, or blocked causing the heart to work harder to pump blood, leading to activity impairment. Although the mean age of diagnosis is between 36 and 50 years, patients of any age may be affected, including pediatric patients. PAH is defined as a mean pulmonary artery pressure (mPAP) > 20 mmHg (at rest) with a pulmonary arterial wedge pressure (PAWP) ≤ 15 mmHg and a pulmonary vascular resistance > 2 Wood units measured by cardiac catheterization.[5] The prognosis in PAH has been described as poor, with the median survival being approximately 3 years. However, primarily due to advances in pharmacological therapies, the long-term prognosis has improved.

Guidelines

Various guidelines address oral prostacyclin products.[3,4] The CHEST guideline and Expert Panel Report regarding therapy for pulmonary arterial hypertension (2019) in adults details many medications.[3] It was cited that many agents with varying mechanisms of action are used for the management of PAH. It was noted that the addition of an oral prostanoid product may be considered in patients with PAH who are in Functional Class III with evidence of rapid disease progression or a poor prognosis among those not willing or able to manage parenteral prostanoids. The European Society of Cardiology and the European Respiratory Society guidelines regarding the treatment of pulmonary hypertension (2022) also recognize Orenitram as having a role in therapy.[4] It may be considered in select patients receiving monotherapy with an endothelin receptor antagonist, phosphodiesterase type 5 inhibitor, or soluble guanylate cyclase stimulator to reduce the risk of morbidity/mortality events.

Safety

Abrupt discontinuation or sudden large reductions in the dosage of Orenitram may cause PAH symptoms to worsen.[1] In the event of a planned short-term treatment interruption for patients unable to take oral medication, consider a temporary infusion of subcutaneous or intravenous treprostinil.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Orenitram. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Orenitram as well as the monitoring required for adverse events and long-term efficacy, approval requires Orenitram to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for initiation of therapy where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes and catheterization laboratory reports. For a patient case in which the documentation requirement of the right heart catheterization upon prior authorization coverage review for a different medication indicated for WHO Group 1 PAH has been previously provided, the documentation requirement in this *Pulmonary Arterial Hypertension – Orenitram Prior Authorization Policy* is considered to be met.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. **Pulmonary Arterial Hypertension (PAH) [World Health Organization {WHO} Group 1].** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and 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 **[documentation required]** (see documentation section above); AND
       - **b)** Results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
     - **iii.** Patient meets ONE of the following (a or b):
       - **a)** Patient has tried or is currently receiving at least one oral medication for PAH from the following different categories (either alone or in combination) each for ≥ 60 days: one phosphodiesterase type 5 (PDE5) inhibitor, one endothelin receptor antagonist (ERA), or Adempas (riociguat tablets); OR
         Note: Examples of phosphodiesterase type 5 inhibitors include sildenafil and tadalafil. Examples of endothelin receptor antagonists include bosentan, ambrisentan, and Opsumit (macitentan tablets). Opsynvi (macitentan/tadalafil tablets) is a combination product containing a phosphodiesterase type 5 inhibitor and endothelin receptor antagonist.
       - **b)** Patient is receiving or has received in the past one PAH prostacyclin therapy or a prostacyclin receptor agonist (i.e., Uptravi [selexipag tablets]) for PAH; AND
         Note: Examples of prostacyclin therapies for PAH include Tyvaso (treprostinil inhalation solution), Tyvaso DPI (treprostinil oral inhalation), Ventavis (iloprost inhalation solution), treprostinil injection, and epoprostenol injection.
     - **iv.** Medication is prescribed by or in consultation with a cardiologist or a pulmonologist.
   - **B)** Patient is Currently Receiving Orenitram. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
     - **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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Orenitram is not recommended in the following situations:

1. **Concurrent Use with Uptravi (selexipag tablets and intravenous infusion), Inhaled Prostacyclin Products, or Parenteral Prostacyclin Agents Used for Pulmonary Hypertension.**
   Note: Examples of medications include Tyvaso (treprostinil inhalation solution), Tyvaso DPI (treprostinil oral inhalation powder), Ventavis (iloprost inhalation solution), epoprostenol intravenous infusion, and treprostinil subcutaneous or intravenous infusion (Remodulin, generic).

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

REFERENCES

1. Orenitram® extended-release tablets [prescribing information]. Research Triangle Park, NC: United Therapeutics; August 2023.
2. Ruopp NF, Cockrill BA. Diagnosis and treatment of pulmonary arterial hypertension. A review. *JAMA*. 2022;327(14):1379-1391.
3. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for pulmonary arterial hypertension in adults. Update of the CHEST guideline and Expert Panel Report. *CHEST*. 2019;155(3):565-586.
4. Humbert M, Kovacs G, Hoeper MM, et al, for the ESC/ERS Scientific Document Group. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;43(38):3618-3731.
5. Maron B. Revised definition of pulmonary hypertension and approach to management: a clinical primer. *J Am Heart Assoc*. 2023 Apr 18;12(8):e029024. [Epub].