VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

TAC APPROVAL DATE: 09/11/2019

OVERVIEW

Orenitram, an oral prostacyclin vasodilator, 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] The studies that established the efficacy of Orenitram included mainly patients with WHO functional class II to III symptoms and etiologies of idiopathic or heritable PAH (66%) or PAH associated with connective tissue disease (26%).

Disease Overview

PAH is a serious but rare condition impacting approximately fewer than 20,000 patients in the US. 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.[2,3] In time, right-sided heart failure and/or death may occur. Common PAH symptoms include shortness of breath, fatigue, chest pain, dizziness and fainting, along with impairment in activity tolerance. It is more prevalent in women. Patients of all ages may develop the disease; however, the mean age of diagnosis typically happens between 36 to 50 years. Children may also have PAH. The condition may occur due to various underlying medical conditions or as a disease that uniquely impacts the pulmonary circulation; both genetic and environmental factors may be involved. PAH is defined as a mean pulmonary artery pressure (mPAP) $\geq$ 25 mmHg with a pulmonary capillary wedge pressure (PCWP) $\leq$ 15 mmHg measured by cardiac catheterization. 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. Lung transplantation may be recommended if pharmacological or medical therapies fail, based upon patient status. The WHO categorizes PAH into stages, which is also referred to as the functional class (Class I to IV) and is an adaptation of the New York Heart Association (NYHA) system to evaluate activity tolerance.

Guidelines

In 2009, the American College of Cardiology Foundation (ACCF) Task Force on Expert Consensus Documents and the American Heart Association (AHA), developed in collaboration with the ACCP, American Thoracic Society (ATS) and the Pulmonary Hypertension Association, published an expert consensus document on pulmonary hypertension.[2] The hemodynamic definition of PAH is a mean pulmonary artery pressure (mPAP) greater than 25 mmHg; a pulmonary capillary wedge pressure (PCWP), left atrial pressure (LAP) or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mmHg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units. Many different medication from varying therapies classes and different routes of administration are recognized. In 2019, and updated CHEST guideline and Expert Panel Report regarding therapy for pulmonary arterial hypertension in adults was released.[3] Many other agents other than Orenitram are recommended as initial and subsequent therapy such as endothelin receptor antagonists (Letairis® [ambrisentan tablets], Tracleer® [bosentan tablets], Opsumit® [macitentan tablets], phosphodiesterase type 5 [PDE 5] inhibitors [tadalafil, sildenafil), and Adempas® (riociguat tablets). The addition of an oral prostanoid product is recommended in patients with PAH who are in Functional Class III without

evidence of rapid disease progression or a poor prognosis among those not willing or able to manage parenteral prostanoids.

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. Because of the specialized skills required for evaluation and diagnosis of patients treated with Orenitram as well as the monitoring required for AEs and long-term efficacy, initial approval requires Orenitram to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 3 years in duration unless otherwise noted below.

Documentation: In the *Pulmonary Arterial Hypertension – Orenitram Prior Authorization Policy*, 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 Indications

1. **Pulmonary Arterial Hypertension (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 3 years if the patient meets all of the following criteria (i, ii, iii, and iv):
     - **i.** The patient has a diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH); AND
     - **ii.** The agent is prescribed by or in consultation with a cardiologist or a pulmonologist; AND
     - **iii.** The patient meets the following criteria (a and b):
       - **a)** The patient has had a right heart catheterization **[documentation required]** (see documentation section above); AND
       - **b)** The results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
     - **iv.** The patient meets one of the following conditions (i or ii):
       - **a)** The patient has tried two oral therapies for PAH (or is currently receiving them) from two of the three 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).

Note: Examples of PDE5 inhibitors include Revatio® (sildenafil tablets and suspension [generic]) and Adcirca® (tadalafil tablets [generic]) and examples of ERAs include Tracleer® (bosentan tablets), Letairis® (ambrisentan tablets [generic]), and Opsumit® (macitentan tablets); OR

b) The patient is receiving or has received in the past for PAH one prostacyclin therapy or a prostacyclin receptor agonist (i.e., Uptravi) for PAH.
Note: Examples of prostacyclin therapies for PAH include Tyvaso® (treprostinil inhalation solution), Ventavis® (iloprost inhalation solution), Remodulin® (treprostinil injection [generic]), and epoprostenol injection [Flolan, Veletri, generics]); OR

B) Patient Currently Receiving Orenitram. Approve for 3 years if the patient meets all of the following criteria (i, ii, and iii):

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

ii. The agent is prescribed by, or in consultation with, a cardiologist or a pulmonologist; AND

iii. The patient meets the following criteria (a and b):

a) The patient has had a right heart catheterization; AND

b) The results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Orenitram has 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. 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 Corporation; October 2019.
2. McLaughlin VV, Archer SL, Badesch DB, et all; Writing committee members. ACCF/AHA 2009 Expert consensus document on pulmonary hypertension: A report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association: Developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *Circulation*. 2009;119:2250-2294.
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.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No criteria changes.	02/08/2017
Annual revision	No criteria changes.	02/14/2018
Annual revision	For initial review, documentation is required for the right heart catheterization. The criteria were deleted regarding patients "who are receiving another medication for WHO Group 1 PAH". For patients who are currently receiving Uptravi, the requirement was added that the patient has had a right heart catheterization and that the results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH. A note was added in the documentation section that 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 is considered to be met.	08/22/2018
Annual revision	No criteria changes. Medications alternatives are now listed in notes.	09/11/2019

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee; WHO – World Health Organization; PAH – Pulmonary arterial hypertension; PDE5 – Phosphodiesterase type 5; ERA – Endothelin receptor antagonist.