PRIOR AUTHORIZATION POLICY

POLICY: Pulmonary Arterial Hypertension – Inhaled Prostacyclin Products
- Ventavis® (iloprost inhalation solution – Actelion)
- Tyvaso® (treprostinil inhalation solution – United Therapeutics)

REVIEW DATE: 09/23/2020

OVERVIEW

Ventavis and Tyvaso are both inhaled prostacyclin vasodilators indicated for the treatment of pulmonary arterial hypertension (PAH).[1,2] Ventavis is indicated for the treatment of PAH (World Health Organization [WHO] Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (based on New York Heart Association [NYHA] Class), and lack of deterioration. Tyvaso is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability.[2]

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.[3,4] 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

An updated treatment algorithm (2013) by the 2nd World Symposium on Pulmonary Hypertension (WSPH) states that patients with Functional Class II should be treated initially with oral therapies (e.g., Adempas® [riociguat tablets], Revatio® (sildenafil tablets and suspension [generics] {Note: brand name Revatio injection also available}), Adcirca® [tadalafil tablets {generic}], Opsumit® [macitentan tablets], Tracleer® [bosentan tablets], and Letairis® [ambrisentan tablets]).[5] Ventavis and Tyvaso are recommended for patients in Functional Class III and IV. In situations of inadequate response, combination therapy (including double or triple therapy) is recommended.

In 2019, and updated CHEST guideline and Expert Panel Report regarding therapy for pulmonary arterial hypertension in adults was released.[4] Evidence for use of the many medications available is also detailed. One recommendation is that parenteral or inhaled prostanoids should not be used as initial therapy for patients with PAH who are treatment naïve with WHO Functional Class II symptoms or as second-line agents for patients with PAH with WHO Functional Class II symptoms who have not met original treatment goals.

POLICY STATEMENT

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

Documentation: In the *Pulmonary Arterial Hypertension – Inhaled Prostacyclin Products 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 – Inhaled Prostacyclin Products Prior Authorization Policy* is considered to be met.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ventavis and Tyvaso is recommended in those who meet the following criteria:

FDA-Approved Indications

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 3 years if the patient meets the following criteria (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 one of the following (a or b):
       - **a)** Patient is in Functional Class III or IV; OR
       - **b)** Patient is in Functional Class II and meets ONE of the following criteria [(1) or (2)]:
         - **(1)** Patient has tried or is currently receiving one oral agent for PAH; OR
           Note: Examples of oral agents for PAH include Tracleer® (bosentan tablets), Letairis® (ambrisentan tablets [generic]), Opsumit® (macitentan tablets), Revatio® (sildenafil tablets and suspension [generics]), Adcirca® (tadalafil tablets [generic]), Alyq™ (tadalafil tablets), Adempas® (riociguat tablets), Orenitram® (treprostinil extended-release tablets), and Uptravi® (selexipag tablets).
         - **(2)** Patient has tried one inhaled or parenteral prostacyclin product for PAH; AND
           Note: Examples of inhaled and parenteral prostacyclin products for PAH include Tyvaso® (treprostinil inhalation solution), Ventavis® (iloprost inhalation solution), Remodulin® (treprostinil injection [generic]), and epoprostenol injection (Flolan®, Veletri®, generics); AND
     - **iii.** 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. Medication is prescribed by, or in consultation with, a cardiologist or a pulmonologist.

B) Patient is Currently Receiving the Requested Inhaled Prostacyclin for PAH (i.e., Ventavis or Tyvaso). Approve for 3 years if the patient meets the following criteria (i, ii, and iii):

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

ii. Patient meets the following criteria (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. Medication is prescribed by, or in consultation with, a cardiologist or a pulmonologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Ventavis and Tyvaso are not recommended in the following situations:

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. Ventavis® inhalation solution [prescribing information]. South San Francisco, CA: Actelion Pharmaceuticals; December 2019.
2. Tyvaso® inhalation solution [prescribing information]. Research Triangle Park, NC: United Therapeutics Corp.; October 2017.
3. McLaughlin VV, Archer SL, Badesch DB, et al. 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. *J Am Coll Cardiol*. 2009;53:1573-1619.
4. 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.
5. Galie N, Corris PA, Frost A, et al. Updated treatment algorithm of pulmonary arterial hypertension. *J Am Coll Cardiol*. 2013;62(25 Suppl):D60-D72.