VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Pulmonary Arterial Hypertension and Related Lung Disease – Inhaled Prostacyclin Products Prior Authorization Policy

- Tyvaso® (treprostinil inhalation solution – United Therapeutics)
- Tyvaso DPI™ (treprostinil oral inhalation powder – MannKind/United Therapeutics)
- Ventavis® (iloprost inhalation solution – Actelion)

REVIEW DATE: 10/06/2021; selected revision 06/08/2022

OVERVIEW

Tyvaso, Tyvaso DPI, and Ventavis are inhaled prostacyclin vasodilators (prostacyclin mimetics) indicated for the treatment of:[1-3]

- **Pulmonary arterial hypertension (PAH), World Health Organization (WHO) Group 1**. Tyvaso and Tyvaso DPI are specifically indicated to improve exercise ability whereas Ventavis is indicated to improve a composite endpoint consisting of exercise tolerance, symptoms, and lack of deterioration.

Tyvaso and Tyvaso DPI are also indicated for:[1,2]

- **Pulmonary hypertension associated with interstitial lung disease (WHO Group 3)**. Tyvaso and Tyvaso DPI are indicated to improve exercise ability for this population.

Disease Overview

PAH is a serious but rare condition impacting approximately fewer than 20,000 patients in the US.[4-6] 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.[4-6] 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 right heart 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.

Pulmonary hypertension due to interstitial lung disease (ILD) [WHO Group 3] can complicate the condition and is associated with an increased need for supplemental oxygen, reduced mobility, and decreased survival.[7-10] Over 80% of patients with ILD can have pulmonary hypertension;[6] patients tend to be older and male. A recent definition is mPAP > 20 mmHg along with a pulmonary vascular resistance of $\geq$ 3 Wood units and a pulmonary artery occlusion pressure $\leq$ 15 mmHg at right-sided heart catheterization in the setting of chronic lung disease. Severe restrictions on pulmonary function tests and marked fibrosis on computed tomography scans are distinctions. The exact etiology is unknown. The symptoms are non-specific and include increased dyspnea on exertion, cough, fatigue, chest pain, and lower extremity edema.

Tyvaso is the only medication indicated for this specific use. Randomized controlled trials utilizing other pulmonary vasodilators indicated for patients with WHO Group 1 PAH in patients with ILD but have not shown clear benefit and some studies suggest harm with use of some medications (e.g., sildenafil, Tracleer® [bosentan tablets], ambrisentan, Adempas® [riociguat tablets], and Opsumit® [macitentan tablets]).

Guidelines

Inhaled prostatcyclin products are included in various guidelines regarding PAH (WHO Group 1).

- **World Symposium on Pulmonary Hypertension (2nd) [2013]:** An updated treatment algorithm by the WSPH states that patients with functional Class II should be treated initially with oral therapies (e.g., Adempas, Revatio® (sildenafil tablets and suspension [generic]), Adcirca® [tadalafil tablets {generic}], Opsumit, Tracleer, 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. Diagnosis is confirmed by a right heart catheterization.
- **CHEST guideline and Expert Panel Report (2019):** Evidence for use of the many medications available is detailed.[6] 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.[6]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Tyvaso, Tyvaso DPI, and Ventavis. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with these products 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 the use of PAH WHO Group 1, 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

I. Coverage of Tyvaso, Tyvaso DPI, and Ventavis 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 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 [generic]), 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), Tyvaso DPI (treprostinil oral inhalation powder), Ventavis (iloprost inhalation solution), Remodulin (treprostinil injection [generic]), and epoprostenol injection (Flolan, Veletri, generic); 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., Tyvaso, Tyvaso DPI, or Ventavis). Approve for 1 year 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.

II. Coverage of Tyvaso and Tyvaso DPI is recommended in those who meet the following criteria:

FDA-Approved Indication

2. Pulmonary Hypertension Associated with Interstitial Lung Disease (World Health Organization [WHO] Group 3). Approve for the duration noted if the patient meets ONE of the following (A or B):
Note: This involves diagnosis such as idiopathic interstitial pneumonia, combined pulmonary fibrosis and emphysema, WHO Group 3 connective disease, and chronic hypersensitivity pneumonitis.
A) Initial Therapy. Approve for 4 months if the patient meets the following criteria (i, ii, iii, iv, v, and vi):
i. Patient is ≥ 18 years of age; AND
ii. Patient has a diagnosis of World Health Organization (WHO) Group 3 interstitial lung disease associated with pulmonary hypertension; AND
iii. Patient with connective tissue disease are required to have a baseline forced vital capacity < 70%; AND
iv. Patient has evidence of diffuse parenchymal lung disease on computed tomography of the chest; AND
v. Patient meets the following criteria (a and b):
a) Patient has had a right heart catheterization **[documentation required]**; AND

b) Results of the right heart catheterization confirm the diagnosis of WHO Group 3 interstitial lung disease associated with pulmonary hypertension; AND

vi. Medication is prescribed by, or in consultation with, a cardiologist or a pulmonologist.

B) Patient is Currently Receiving Tyvaso or Tyvaso DPI for pulmonary hypertension associated with interstitial lung disease. Approve for 1 year if the patient meets the following criteria (i, ii, iii, iv and v):

i. Patient is ≥ 18 years of age; AND

ii. Patient has a diagnosis of World Health Organization (WHO) Group 3 interstitial lung disease associated with pulmonary hypertension; AND

iii. 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 World Health Organization (WHO) Group 3 interstitial lung disease associated with pulmonary hypertension; AND

iv. Patient has had a response to therapy according to the prescriber.
Note: Examples of a response include an increase or maintenance in the six-minute walk distance from baseline, improved exercise capacity, decrease in N-terminal pro-B-type natriuretic peptide levels, lessened clinical worsening, and a reduced rate of exacerbations of underlying lung disease.

v. Medication is prescribed by, or in consultation with, a cardiologist or a pulmonologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Tyvaso, Tyvaso DPI, and Ventavis 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. Tyvaso® inhalation solution [prescribing information]. Research Triangle Park, NC: United Therapeutics; March 2021.
2. Tyvaso DPI™ oral inhalation powder [prescribing information]. Danbury, CT and Research Triangle Park, NC: MannKind and United Therapeutics; May 2022.
3. Ventavis® inhalation solution [prescribing information]. South San Francisco, CA: Actelion; January 2021.
4. 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.
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.
6. 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.
7. Waxman A, Restrepp-Jaramillo R, Thenappan T, et al. Inhaled treprostinil in pulmonary hypertension due to interstitial lung disease. *N Engl J Med*. 2021;384:325-334.
8. King CS, Nathan SD. Pulmonary hypertension due to interstitial lung disease. *Curr Opin Pulm Med*. 2019;25:459-467.
9. King CS, Shlobin OA. The trouble with Group 3 pulmonary hypertension in interstitial lung disease. Dilemmas in diagnosis and the conundrum of treatment. *CHEST*. 2020;158(4):1651-1664.
10. Shioleno AM, Ruopp NF. Group 3 pulmonary hypertension: a review of diagnostics and clinical trials. *Clin Chest Med*. 2021;42:59-70.

HISTORY

Type of Revision	Summary of Changes	Review Date

Annual Revision	No criteria changes. Alyq (tadalafil tablets) listed as an example of an oral medication for pulmonary arterial hypertension in a Note.	09/23/2020
Selected Revision	**Interstitial Lung Disease Associated Pulmonary Hypertension (World Health Organization [WHO] Group 3):** Criteria for Tyvaso were developed for this new indication added to the policy, which was recently FDA-approved.	05/12/2021
Annual Revision	No criteria changes.	10/06/2021
Selected Revision	The phrase "and Related Lung Disease" was added to the header of the Policy which previously stated "Pulmonary Arterial Hypertension". In addition, the following criteria changes were made: **Pulmonary Arterial Hypertension [World Health Organization Group 1].** Tyvaso DPI was added to the policy and a patient must meet the previously established criteria for this condition. Also, Tyvaso DPI was added in the Note which lists examples of examples of inhaled prostacyclin products used for pulmonary arterial hypertension. The duration of therapy for initial therapy for a patient currently receiving the requested inhaled prostacyclin product was changed from 3 years to 1 year. **Interstitial Lung Disease Associated Pulmonary Hypertension (World Health Organization [WHO] Group 3):** Tyvaso DPI was added to the policy and a patient must meet the previously established criteria that was in place for Tyvaso.	06/08/2022