MEDICAL MUTUAL®

Drug Policy

Policy:	**201807**	**Initial Effective Date: 04/28/2014**
Code(s):	**HCPCS Q4074, J7686, J8499**	**Annual Review Date: 02/20/2025**
SUBJECT:	**Pulmonary Arterial Hypertension – Inhaled Prostacyclin Products** **Ventavis® (iloprost inhalation solution)*** **Tyvaso® (treprostinil inhalation solution)** **Tyvaso DPI (Treprostinil inhalation powder)**	**Last Revised Date: 02/20/2025**

Subject to: ☒Site of Care
☐Medication Sourcing

***MMO requires that prior Authorization requests for Ventavis are submitted under the medical benefit.**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

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.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

Policy Statement

This policy involves the use of inhaled prostacyclin. Prior authorization is recommended for pharmacy and medical benefit coverage of inhaled prostacyclin. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section.

Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with inhaled prostacyclin as well as the monitoring required for AEs and long-term efficacy, initial approval requires inhaled prostacyclin be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

The Site of Care Medical Necessity Criteria applies to initial therapy and reauthorizations under the medical benefit.

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 policy is considered to be met.

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 1 year if the patient meets 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 ONE of the following criteria (a or b):
       - **a)** The patient is in Functional Class III or IV; OR
       - **b)** The patient is in Functional Class II and meets ONE of the following criteria [(1) or (2)]:
         - **(1)** The patient has tried or is currently receiving one oral agent for PAH (e.g., Tracleer [bosentan tablets], Letairis® [ambrisentan tablets], Opsumit® [macitentan tablets], Revatio® [sildenafil tablets {generic} and suspension], Adcirca® [tadalafil tablets] {generic}), Adempas® [riociguat tablets], Orenitram™ [treprostinil extended-release tablets], or Uptravi® [selexipag tablets]); OR
         - **(2)** The patient has tried one inhaled or parenteral prostacyclin product for PAH (e.g., Tyvaso™ [treprostinil inhalation solution], Tyvaso DPI (treprostinil oral inhalation powder), Ventavis® [iloprost inhalation solution], Remodulin® [treprostinil injection], epoprostenol injection [Flolan®, Veletri®, generics]); AND.
     - **iv.** 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; OR

B) Patients Currently Receiving the Requested Inhaled Prostacyclin for PAH (i.e., Ventavis or Tyvaso). Approve for 1 year if the patient meets 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
Note: This refers to prior to starting therapy with a medication for WHO Group 1 PAH.

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

Dosing of Ventavis in Pulmonary Arterial Hypertension (PAH). *Dosing must meet the following*:
Ventavis is intended to be inhaled using the I-neb® AAD® System. The first inhaled dose should be 2.5 mcg (as delivered at the mouthpiece). If this dose is well tolerated, dosing should be increased to 5.0 mcg and maintained at that dose; otherwise maintain the dose at 2.5 mcg. Ventavis should be taken 6 to 9 times per day (no more than once every 2 hours) during waking hours, according to individual need and tolerability. The maximum daily dose evaluated in clinical studies was 45 mcg (5 mcg 9 times per day).

Dosing of Tyvaso in Pulmonary Arterial Hypertension (PAH). *Dosing must meet the following*:
Tyvaso inhalation solution Initial Dosage:
Therapy should begin with 3 breaths of Tyvaso (18 mcg of treprostinil), per treatment session, 4 times daily. If 3 breaths are not tolerated, reduce to 1 or 2 breaths and subsequently increase to 3 breaths, as tolerated.

Tyvaso DPI inhalation powder Initial Dosage:
Tyvaso DPI therapy should begin with one 16 mcg cartridge per treatment session, four time daily.

Tyvaso inhalation solution Maintenance Dosage:
Dosage should be increased by an additional 3 breaths at approximately 1-to-2-week intervals, if tolerated, until the target dose of 9 breaths (54 mcg of treprostinil) is reached per treatment session, 4 times daily. If adverse effects preclude titration to target dose, Tyvaso should be continued at the highest tolerated dose.
If a scheduled treatment session is missed or interrupted, therapy should be resumed as soon as possible at the usual dose. The maximum recommended dosage is 9 breaths per treatment session, 4 times daily.

Tyvaso DPI inhalation powder Maintenance Dosage:
Increase dosage be an additional 16 mcg per treatment session at approximately 1-to-2-week intervals. The target maintenance dosage is usually 48 mcg to 64 mcg per session. If adverse effects preclude titration to target dose, Tyvaso should be continued at the highest tolerated dose. If a scheduled treatment session is missed or interrupted, therapy should be resumed as soon as possible at the usual dose.

2. **Pulmonary Hypertension Associated with Interstitial Lung Disease (World Health Organization [WHO] Group 3).** ***[T*** 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 Tyvaso 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 pulmonary hypertension associated with interstitial lung disease; AND
      iii. Patient with connective tissue disease is 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 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
         Note: This refers to prior to starting therapy with a medication for WHO Group 3 PAH.
         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; AND
         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.

Dosing of Tyvaso in Interstitial Lung Disease Associated Pulmonary Hypertension. *Dosing must meet the following*:
Tyvaso inhalation solution Initial Dosage:
Therapy should begin with 3 breaths of Tyvaso (18 mcg of treprostinil), per treatment session, 4 times daily. If 3 breaths are not tolerated, reduce to 1 or 2 breaths and subsequently increase to 3 breaths, as tolerated.

Tyvaso DPI inhalation powder Initial Dosage:
Tyvaso DPI therapy should begin with one 16 mcg cartridge per treatment session, four time daily.

Tyvaso inhalation solution Maintenance Dosage:

Dosage should be increased by an additional 3 breaths at approximately 1-to-2-week intervals, if tolerated, until the target dose of 9 breaths (54 mcg of treprostinil) is reached per treatment session, 4 times daily. If adverse effects preclude titration to target dose, Tyvaso should be continued at the highest tolerated dose.
If a scheduled treatment session is missed or interrupted, therapy should be resumed as soon as possible at the usual dose.
The maximum recommended dosage is 9 breaths per treatment session, 4 times daily.

Tyvaso DPI inhalation powder Maintenance Dosage:
Increase dosage be an additional 16 mcg per treatment session at approximately 1-to-2-week intervals. The target maintenance dosage is usually 48 mcg to 64 mcg per session. If adverse effects preclude titration to target dose, Tyvaso should be continued at the highest tolerated dose. If a scheduled treatment session is missed or interrupted, therapy should be resumed as soon as possible at the usual dose.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Ventavis and Tyvaso have 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.

1. **Concurrent Use with Oral or Parenteral Prostacyclin Agents Used for Pulmonary Hypertension.** Concomitant use is not recommended.
   Note: Examples of medications include Orenitram (treprostinil extended-release tablets), Uptravi (selexipag tablets and intravenous infusion), 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.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

References

1. TyvasoÒ inhalation solution [prescribing information]. Research Triangle Park, NC: United Therapeutics; May 2022.
2. Tyvaso DPI™ oral inhalation powder [prescribing information]. Danbury, CT and Research Triangle Park, NC: MannKind and United Therapeutics; June 2023.
3. VentavisÒ inhalation solution [prescribing information]. South San Francisco, CA: Actelion; March 2022.
4. Ruopp NF, Cockrill BA. Diagnosis and treatment of pulmonary arterial hypertension. A review. JAMA. 2022;327(14):1379-1391.
5. 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.
6. 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.
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.
11. Maron BA. Revised Definition of Pulmonary Hypertension and Approach to Management: A Clinical Primer. J Am Heart Assoc. 2023 Apr 18;12(8):e029024. [Epub].

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J7686, Q4074, J8499

Edits and Denials:

Prior approval: Prior approval is required for iloprost **(HCPCS Code J7686, Q4074, J8499)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within the Corporate Medical Policy.