

Medical Drug Clinical Criteria

Subject: Prostacyclin Infusion and Inhalation Therapy

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Overview

This document addresses the use of intravenous, subcutaneous and inhalation administration of prostacyclin analogues approved by the Food and Drug Administration (FDA) for the treatment of pulmonary arterial hypertension including:

- Flolan (epoprostenol) via continuous intravenous infusion
- Remodulin (treprostinil) via continuous subcutaneous or intravenous infusion
- Tyvaso (treprostinil) via inhalation
- Veletri (epoprostenol) via continuous intravenous infusion
- Ventavis (iloprost) via inhalation
- Yutrepla (treprostinil) via inhalation

Pulmonary arterial hypertension (PAH) is a life-threatening disease characterized by sustained elevations of the mean pulmonary artery pressure (mPAP), thickening of the pulmonary arteries and narrowing of the blood vessels. As the disease progresses, the right side of the heart becomes enlarged and may fail. Right heart catheterization is essential to confirm a diagnosis. PAH is defined by the 2009 American College of Cardiology Foundation and the American Heart Association (ACCF/AHA) Expert Consensus Document on Pulmonary Hypertension (McLaughlin 2009) and by updated specialty society guidelines for adults and children (2013 ACCF Hoeper; 2013 ACCF Ivy; 2015 AHA/ATS Abman) as all of the following:

1. Mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest;
2. Pulmonary capillary wedge pressure (PCWP), mean pulmonary artery wedge pressure (PAWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg;
3. Pulmonary vascular resistance (PVR) greater than 3 Wood units.

Agents approved by the FDA to treat PAH were studied in populations meeting these right heart catheterization diagnostic parameters. The 6th World Symposium on Pulmonary Hypertension (Simonneau 2019) proposed updating the definition of pulmonary hypertension to include individuals with a mPAP greater than 20 mm Hg and a PVR greater than 2 Wood units. The guidance did note that prospective clinical trials would be needed to determine if individuals meeting the expanded PAH definition would benefit from currently approved PAH treatments. The 7th World Symposium (Kovacs 2024) confirmed both the new PAH definition and the need for additional clinical studies in individuals meeting the expanded definition.

Medical management of PAH consists of diuretics, supplemental oxygen, anticoagulants, calcium channel blockers, phosphodiesterase-5 (PDE-5) inhibitors, endothelin receptor antagonists (ERA), soluble guanylate cyclase stimulators, prostacyclin receptor agonists, activin signaling inhibitors and oral, inhaled or infused prostacyclin analogs. There are no direct comparisons between products in the literature, making it difficult to support the use of one drug over another in terms of efficacy. Some safety parameters and administration issues do differ between products. As a result, treatment choices should be individualized. Lung or heart-lung transplantation has been performed in individuals who are refractory to medical management.

The clinical effectiveness and safety of infusion and inhalation of prostacyclin analogs for treatment of individuals with idiopathic pulmonary arterial hypertension (IPAH) or PAH associated with connective tissue disorders or congenital heart defects is well documented in the peer-reviewed medical literature. These therapies improve cardiopulmonary hemodynamics, exercise tolerance and quality of life in many individuals. All prostacyclin analogs are approved by the FDA to treat PAH World Health Organization (WHO) Group 1. Flolan, Veletri and Ventavis are approved for individuals with New York Heart Association (NYHA) Functional Class III or IV symptoms. Remodulin is approved for individuals with NYHA Class II, III or IV symptoms. Tyvaso is only approved for individuals with NYHA Class III symptoms.

Remodulin was originally approved as a subcutaneous infusion. The FDA subsequently approved intravenous use of Remodulin for individuals unable to tolerate subcutaneous infusion. Due to the shorter half-life of Remodulin when given intravenously as compared to

subcutaneously, the intravenous route may increase the risks related to abrupt cessation in the delivery of the medication as occurs with pump malfunction. Accordingly, Remodulin is preferably infused subcutaneously but can be administered by a central intravenous line if the subcutaneous route is not tolerated due to severe site pain or reaction.

In 2007, the American College of Chest Physicians (ACCP) clinical practice guidance (Badesch 2007) recommended that for individuals with a favorable response to acute vasodilator challenge, treatment with an oral calcium channel blocker should be considered prior to the use of prostacyclin analogs. The guidelines defined an acute response to vasodilators as a fall in mPAP of at least 10 mm Hg to 40 mm Hg or lower with an unchanged or increased cardiac output when challenged with inhaled nitric oxide, intravenous epoprostenol or intravenous adenosine. The 6th World Symposium on Pulmonary Hypertension (Simonneau 2019) confirms vasoreactivity testing and includes inhaled iloprost as another option for testing. If a calcium channel blocker is used, close follow-up is recommended with reassessment after three months to verify that the individual has improved to NYHA Functional Class I or II.

In 2019, updated CHEST guidelines on pulmonary arterial hypertension therapy were published (Klinger 2019). The 2019 guidance primarily reaffirms the 2014 CHEST guidance but with a new focus on combination therapy in certain clinical situations. A trial of oral calcium channel blocker therapy is recommended for individuals who demonstrate acute vasoreactivity. The guidance recommends treatment naïve individuals with functional class II and III symptoms initiate therapy with Letairis in combination with Adcirca. If an individual cannot tolerate dual therapy, the guidelines recommend monotherapy with an ERA, PDE-5 inhibitor or a soluble guanylate cyclase stimulator. The guidance recommends initiating therapy with a parenteral prostacyclin for individuals with functional class IV symptoms.

In 2024, the 7th World Symposium published a treatment algorithm for pulmonary hypertension (Chin 2024). For low-risk individuals, the guidelines recommend a combination of an ERA and a PDE-5 inhibitor. High-risk individuals require more aggressive strategies including a combination of parenteral prostacyclin, ERA and PDE-5 inhibitor. Frequent reassessment of risk is stressed and escalation to three or four drugs in combination is recommended for anyone who is not at low risk.

Tyvaso has an additional FDA indication for the treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability. The efficacy of Tyvaso was demonstrated in a randomized, double-blind, placebo-controlled trial in 326 individuals with interstitial lung disease and group 3 pulmonary hypertension. The study primarily included individuals with idiopathic interstitial pneumonia (IIP) (45%) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE) (25%) and WHO Group 3 connective tissue disease (22%). Diagnosis was confirmed via computed tomography of the chest and right-heart catheterization. At week 16, the difference in change from baseline 6-minute walk distance between the Tyvaso and placebo groups was 31.12 ± 7.25 meters ($P < 0.001$).

Comprehensive Clinical Classification of Pulmonary Hypertension (PH) (CHEST 2019)

1. PAH
 - 1.1 Idiopathic PAH
 - 1.2 Heritable PAH
 - 1.2.1 *BMPR2*
 - 1.2.2 *ALK-1, ENG, SMAD9, CAV1, KCNK3*
 - 1.2.3 Unknown
 - 1.3 Drug and toxin induced
 - 1.4 Associated with:
 - 1.4.1 Connective tissue disease
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
 - 1'. Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis
 - 1'.1 Idiopathic
 - 1'.2 Heritable
 - 1'.2.1 *EIF2AK4* mutation
 - 1'.2.2 Other mutations
 - 1'.3 Drugs, toxins, and radiation induced
 - 1'.4 Associated with:
 - 1'.4.1 Connective tissue disease
 - 1'.4.2 HIV infection
 - 1". Persistent pulmonary hypertension of the newborn
 2. Pulmonary hypertension because of left heart disease
 - 2.1 Left ventricular systolic dysfunction
 - 2.2 Left ventricular diastolic dysfunction
 - 2.3 Valvular disease
 - 2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
 3. Pulmonary hypertension because of lung diseases and/or hypoxia
 - 3.1 COPD
 - 3.2 Interstitial lung disease

- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental lung diseases
- 4. Chronic thromboembolic pulmonary hypertension
 - 4.1 Chronic thromboembolic pulmonary hypertension
 - 4.2 Other pulmonary artery obstructions
 - 4.2.1 Angiosarcoma
 - 4.2.2 Other intravascular tumors
 - 4.2.3 Arteritis
 - 4.2.4 Congenital pulmonary arteries
 - 5. Pulmonary hypertension with unclear multifactorial mechanisms
 - 5.1 Hematologic disorders: chronic hemolytic anemia, myeloproliferative disorders, splenectomy
 - 5.2 Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
 - 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
 - 5.4 Others: tumoral

New York Heart Association (NYHA) Functional Classification for Heart Failure symptoms:

Class I	No limitation with ordinary physical activity
Class II	Slight limitation with fatigue, dyspnea, palpitations, or angina resulting from ordinary physical activity
Class III	Marked limitation; symptomatic with less than ordinary activity
Class IV	Symptoms present while at rest

Tyvaso DPI Titration Kit 16 mcg-32 mcg and Maintenance Kit 32 mcg-48 mcg were discontinued by the manufacturer. Criteria will remain active until March 2026 and May 2025 as claims can adjudicate several years after agent discontinuation.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Epoprostenol Agents (Flolan, Veletri)

Initial requests for continuous intravenous infusion epoprostenol (Flolan, Veletri) may be approved if the following criteria are met:

- I. Individual has a diagnosis of pulmonary arterial hypertension (PAH) and a right-heart catheterization showing all of the following (Hooper, 2013; Ivy, 2013; Abman, 2015):
 - A. Mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest;
 - B. Pulmonary capillary wedge pressure (PCWP), mean pulmonary artery wedge pressure (PAWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg;
 - C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

- II. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects, and all Group 1 subtypes);

AND

- III. Individual has New York Heart Association Functional Class III or IV symptoms.

Continuation requests for continuous intravenous infusion epoprostenol (Flolan, Veletri) may be approved if the following criterion is met:

- I. There is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improvement in walk distance, dyspnea and/or functional class).

Continuous intravenous infusion epoprostenol (Flolan, Veletri) may not be approved for the following:

- I. Individual with WHO Group II-V pulmonary hypertension; **OR**
- II. Individuals with heart failure due to severe left ventricular systolic dysfunction; **OR**
- III. In combination with other prostacyclin analogs [including but not limited to treprostinil (Orenitram, Remodulin, Tyvaso, **Yutrepla**), Ventavis (iloprost)] or prostacyclin receptor agonists [including but not limited to Uptravi (selexipag)]; **OR**
- IV. May not be approved when the above criteria are not met and for all other indications.

Remodulin (treprostинil)

Initial requests for continuous subcutaneous infusion of Remodulin (treprostинil) may be approved if the following criteria are met:

- I. Individual has a diagnosis of pulmonary arterial hypertension (PAH) and a right-heart catheterization showing all of the following (Hooper, 2013; Ivy, 2013; Abman, 2015):
 - A. Mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest;
 - B. Pulmonary capillary wedge pressure (PCWP), mean pulmonary artery wedge pressure (PAWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg;
 - C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

- II. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects, and all Group 1 subtypes);

AND

- III. Individual has New York Heart Association Functional Class II, III or IV symptoms.

Continuation requests for continuous subcutaneous infusion of Remodulin (treprostинil) may be approved if the following criterion is met:

- I. There is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improvement in walk distance, dyspnea and/or functional class).

Initial requests for continuous intravenous infusion of Remodulin (treprostинil) may be approved if the following criteria are met:

- I. Individual has a diagnosis of pulmonary arterial hypertension (PAH) and a right-heart catheterization showing all of the following (Hooper, 2013; Ivy, 2013; Abman, 2015):
 - A. Mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest;
 - B. Pulmonary capillary wedge pressure (PCWP), mean pulmonary artery wedge pressure (PAWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg;
 - C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

- II. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects, and all Group 1 subtypes);

AND

- III. Individual has New York Heart Association Functional Class II, III or IV symptoms;

AND

- IV. Individual has inability to tolerate treatment by subcutaneous infusion of Remodulin.

Continuation requests for continuous intravenous infusion of Remodulin (treprostинil) may be approved if the following criterion is met:

- I. There is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improvement in walk distance, dyspnea and/or functional class).

Continuous subcutaneous or intravenous infusion of Remodulin (treprostинil) may not be approved for the following:

- I. Individual with WHO Group II-V pulmonary hypertension; **OR**
- II. In combination with other prostacyclin analogs [including but not limited to epoprostenol (Flolan, Veletri), Ventavis (iloprost)] or prostacyclin receptor agonists [including but not limited to Uptravi (selexipag)]; **OR**
- III. In combination with other treprostинil dosage forms (oral, inhalation) unless transitioning from one dose form to another; **OR**
- IV. May not be approved when the above criteria are not met and for all other indications.

Tyvaso (treprostинil)

Initial requests for inhalation therapy with Tyvaso (treprostинil) may be approved if the following criteria are met:

- I. Individual has a diagnosis of pulmonary arterial hypertension (PAH) and a right-heart catheterization showing all of the following (Hooper, 2013; Ivy, 2013; Abman, 2015):
 - A. Mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest;
 - B. Pulmonary capillary wedge pressure (PCWP), mean pulmonary artery wedge pressure (PAWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg;
 - C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

- II. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects, and all Group 1 subtypes);

AND

- III. Individual has New York Heart Association Functional Class III or IV symptoms;

OR

- IV. Individual has a diagnosis of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3); **AND**

- V. Diagnosis is demonstrated by (Waxman 2021):

- A. Right-heart catheterization showing all of the following:

- 1. Mean pulmonary arterial pressure (mPAP) greater than or equal to 25 mm Hg;
- 2. Pulmonary capillary wedge pressure (PCWP) less than or equal to 15 mm Hg;
- 3. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

- B. Chest high resolution computed tomography (HRCT) showing diffuse parenchymal lung disease.

Continuation requests for Tyvaso (treprostинil) may be approved if the following criterion is met:

- I. There is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improvement in walk distance, dyspnea and/or functional class).

Inhalation therapy with Tyvaso (treprostинil) may not be approved for the following:

- I. Individual with WHO Group II, IV or V pulmonary hypertension; **OR**

- II. In combination with other prostacyclin analogs [including but not limited to epoprostenol (Flolan, Veletri), treprostинil (Orenitram, Remodulin, **Yutreпia**), Ventavis (iloprost)] or prostacyclin receptor agonists [including but not limited to Uptravi (selexipag)]; **OR**

- III. May not be approved when the above criteria are not met and for all other indications.

Yutreпia (treprostинil)

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Initial requests for inhalation therapy with Yutreпia (treprostинil) may be approved if the following criteria are met:

- I. Individual has a diagnosis of pulmonary arterial hypertension (PAH) and a right-heart catheterization showing all of the following (Hooper 2013; Ivy 2013; Abman 2015):

- A. Mean pulmonary arterial pressure (mPAP) greater than or equal to 25 mm Hg at rest;
- B. Pulmonary capillary wedge pressure (PCWP), mean pulmonary arterial wedge pressure (PAWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg;
- C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

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AND

- II. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects and all Group 1 subtypes); **AND**

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- III. Individual has New York Heart Association Functional Class III or IV symptoms;

OR

- IV. Individual has a diagnosis of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3); **AND**

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- V. Diagnosis is demonstrated by (Waxman 2021):

- A. Right-heart catheterization showing all of the following:

- 1. Mean pulmonary arterial pressure (mPAP) greater than or equal to 25 mm Hg;
- 2. Pulmonary capillary wedge pressure (PCWP) less than or equal to 15 mm Hg;
- 3. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

- B. Chest high resolution computed tomography (HRCT) showing diffuse parenchymal lung disease.

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Continuation requests for Yutreпia (treprostинil) may be approved if the following criterion is met:

- I. There is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improvement in walk distance, dyspnea and/or functional class).

Inhalation therapy with Yutreпia (treprostинil) may not be approved for the following:

- I. Individual with WHO Group II, IV or V pulmonary hypertension; **OR**

- II. In combination with other prostacyclin analogs [including but not limited to epoprostenol (Flolan, Veletri), treprostинil (Orenitram, Remodulin, Tyvaso), Ventavis (iloprost)] or prostacyclin receptor agonists [including but not limited to Uptravi (selexipag)]; OR
- III. May not be approved when the above criteria are not met and for all other indications.

Ventavis (iloprost)

Initial requests for inhalation therapy with Ventavis (iloprost) may be approved if the following criteria are met:

- I. Individual has a diagnosis of pulmonary arterial hypertension (PAH) and a right-heart catheterization showing all of the following (Hoeper 2013; Ivy 2013; Abman 2015):
 - A. Mean pulmonary arterial pressure (mPAP) greater than or equal to 25 mm Hg at rest;
 - B. Pulmonary capillary wedge pressure (PCWP), mean pulmonary arterial wedge pressure (PAWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg;
 - C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

- II. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects and all Group 1 subtypes); **AND**
- III. Individual has New York Heart Association Functional Class III or IV symptoms.

Continuation requests for Ventavis (iloprost) may be approved if the following criterion is met:

- I. There is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improvement in walk distance, dyspnea and/or functional class).

Inhalation therapy with Ventavis (iloprost) may not be approved for the following:

- I. Individual with WHO Group II-V pulmonary hypertension; **OR**
- II. In combination with other prostacyclin analogs [including but not limited to epoprostenol (Flolan, Veletri), treprostинil (Orenitram, Remodulin, Tyvaso, Yutrepla)] or prostacyclin receptor agonists [including but not limited to Uptravi (selexipag)]; **OR**
- III. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Tyvaso (treprostинil) and Ventavis (iloprost) Quantity Limits

Drug	Limit
Tyvaso (treprostинil) Inhalation System Starter Kit	1 kit, one time fill
Tyvaso (treprostинil) Inhalation System Refill Kit	1 kit per 28 days
Tyvaso (treprostинil) 1.74 mg/2.9 mL (0.6 mg/mL) ampule	1 ampule per day
Tyvaso DPI (treprostинil) Inhalation Powder Titration Kit (112 16 mcg cartridges, 84 32 mcg cartridges)	1 kit, one time fill
Tyvaso DPI (treprostинil) Inhalation Powder Titration Kit (112 16 mcg cartridges, 112 32 mcg cartridges, 28 48 mcg cartridges)	1 kit, one time fill
Tyvaso DPI (treprostинil) Inhalation Powder Maintenance Kit (112 16 mcg cartridges)	1 kit per 28 days
Tyvaso DPI (treprostинil) Inhalation Powder Maintenance Kit (112 32 mcg cartridges)	1 kit per 28 days
Tyvaso DPI (treprostинil) Inhalation Powder Maintenance Kit (112 48 mcg cartridges)	1 kit per 28 days
Tyvaso DPI (treprostинil) Inhalation Powder Maintenance Kit (112 64 mcg cartridges)	1 kit per 28 days
Tyvaso DPI (treprostинil) Inhalation Powder Maintenance Kit (112 32 mcg cartridges, 112 48 mcg cartridges)	1 kit per 28 days
Ventavis (iloprost) 10 mcg/mL, 20 mcg/mL ampule	9 ampules per day
<u>Yutrepla (treprostинil) 26.5 mcg</u>	<u>5 capsules per day</u>
<u>Yutrepla (treprostинil) 53 mcg</u>	<u>5 capsules per day</u>
<u>Yutrepla (treprostинil) 79.5 mcg</u>	<u>10 capsules per day</u>
<u>Yutrepla (treprostинil) 106 mcg</u>	<u>8 capsules per day</u>

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement

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policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

[Flolan, Veletri \(epoprostenol\); Remodulin \(treprostinil\); Ventavis \(iloprost\)](#)

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HCPCS

J3125	Injection, epoprostenol; 0.5 mg [Flolan, Veletri]
J3285	Injection, treprostinil, 1 mg [Remodulin]
J7686	Treprostinil, inhalation solution, FDA-approved final product, non-compounded, administered through DME, unit dose form, 1.74 mg [TYVASO]
K0455	Infusion pump used for uninterrupted parenteral administration of medication (e.g., epoprostenol or treprostinil)
Q4074	Iloprost, inhalation solution, FDA-approved final product, non-compounded, administered through DME, unit dose form, up to 20 micrograms [Ventavis]
S0155	Sterile dilutant for epoprostenol, 50 ml [dilutant for Flolan]
S9347	Home infusion therapy, uninterrupted, long-term, controlled rate intravenous or subcutaneous infusion therapy (e.g., epoprostenol)

ICD-10 Diagnosis

I27.0	Primary pulmonary hypertension [Flolan, Veletri, Remodulin, Tyvaso, Ventavis]
I27.20	Pulmonary hypertension, unspecified [Flolan, Veletri, Remodulin, Tyvaso, Ventavis]
I27.21	Secondary pulmonary arterial hypertension [Flolan, Veletri, Remodulin, Tyvaso, Ventavis]
<u>I27.23</u>	<u>Pulmonary hypertension due to lung diseases and hypoxia [Tyvaso only]</u>
I27.83	Eisenmenger's syndrome [Flolan, Veletri, Remodulin, Tyvaso, Ventavis]
I27.89	Other specified pulmonary heart diseases [Flolan, Veletri, Remodulin, Tyvaso, Ventavis]
I27.9	Pulmonary heart disease, unspecified [Flolan, Veletri, Remodulin, Tyvaso, Ventavis]
M34.0	Progressive systemic sclerosis [Flolan, Veletri, Remodulin, Tyvaso, Ventavis]
<u>M34.81</u>	<u>Systemic sclerosis with lung involvement [Tyvaso only]</u>
M34.9	Systemic sclerosis, unspecified [Flolan, Veletri, Remodulin, Tyvaso, Ventavis]
Q20.0-Q24.9	Congenital malformations of heart [Flolan, Veletri, Remodulin, Tyvaso, Ventavis]

[Tyvaso \(treprostinil inhalation solution\); Yutrepxia \(treprostinil inhalation powder\)](#)

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HCPCS

J7686	Treprostinil, inhalation solution, FDA-approved final product, noncompounded, administered through DME, unit dose form, 1.74 mg [Tyvaso]
J8499	Prescription drug, oral, non-chemotherapeutic, NOS [when specified as Yutrepxia (treprostinil inhalation powder)]

ICD-10 Diagnosis

I27.0	<u>Primary pulmonary hypertension</u>
I27.20	<u>Pulmonary hypertension, unspecified</u>
I27.21	<u>Secondary pulmonary arterial hypertension</u>
<u>I27.23</u>	<u>Pulmonary hypertension due to lung diseases and hypoxia</u>
I27.83	<u>Eisenmenger's syndrome</u>
I27.89	<u>Other specified pulmonary heart diseases</u>
I27.9	<u>Pulmonary heart disease, unspecified</u>
M34.0	<u>Progressive systemic sclerosis</u>
<u>M34.81</u>	<u>Systemic sclerosis with lung involvement</u>
M34.9	<u>Systemic sclerosis, unspecified</u>

Document History

Revised: 9/8/2025

Document History:

- 9/8/2025 – Select Review: Add clinical criteria and quantity limit for Yutrepla. Update may not be used in combination criteria to include Yutrepla. Coding Reviewed: Added HCPCS NOC J8499 for Yutrepla. Grouped agents according to ICD-10-CM codes. Added ICD-10-CM I27.0, I27.20, I27.21, I27.23, I27.83, I27.89, I27.9, M34.0, M34.81, M34.9, Q20.0-Q24.9 to Yutrepla.
- 2/21/2025 – Annual Review: No changes. Coding Reviewed: Updated description for HCPCS S9347. Added ICD-10-CM I27.23. Added drug names to applicable ICD-10-CM codes.
- 2/23/2024 – Annual Review: Add quantity limit. Coding Reviewed: No changes.
- 2/24/2023 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 6/13/2022 – Select Review: Update all criteria by removing vasodilatory testing and trial of calcium channel blocker requirements. Coding Reviewed: No changes.
- 2/25/2022 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 6/14/2021 – Select Review: Separate Tyvaso and Ventavis criteria. Update Tyvaso criteria for PH-ILD indication. Update list of concomitant agent exclusions in Tyvaso and Ventavis criteria. Coding Reviewed: No changes.
- 2/19/2021 – Annual Review: Update vasoreactivity testing criteria for Flolan, Veletri, Remodulin, Tyvaso and Ventavis; add continuation criteria; add may not approve criteria for combination with other prostacyclin analogs or prostacyclin receptor agonists. Coding Reviewed: No changes.
- 2/21/2020 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 2/22/2019 – Annual Review: Update WHO Group language in Epoprostenol Agents, Remodulin and Tyvaso and Ventavis criteria.
- 11/16/2018 – Select Review: Initial P&T review of Prostacyclin Infusion and Inhalation Therapy Clinical Guideline. Add may not approve criteria for individuals with heart failure due to severe left ventricular systolic dysfunction in the Flolan and Veletri clinical guideline based on labeled contraindication. Wording and formatting updates for clarity. Add references for non-label-based criteria elements. HCPCS Code Review: no change. ICD-10 Coding Review: no change.

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