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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Cardiovascular Agents	**Original Policy Date:**	June 9, 2011
Subject:	Tyvaso	**Page:**	1 of 7

Last Review Date: March 7, 2025

Tyvaso

Description

Tyvaso (treprostinil)

Background
Tyvaso (treprostinil) is a prostacyclin analogue. Tyvaso's major pharmaceutical actions are direct vasodilation of pulmonary and systemic arterial vascular beds and inhibition of platelet aggregation. Tyvaso is indicated for the treatment of pulmonary hypertension (1).

The World Health Organization (WHO) has classified pulmonary hypertension into five different groups: (2)

WHO Group 1: Pulmonary Arterial Hypertension (PAH)
1.1 Idiopathic (IPAH)
1.2 Heritable PAH
- 1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
- 1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
- 1.2.3 Unknown

1.3 Drug and toxin-induced
1.4 Associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases

1.4.5 Schistosomiasis

1'. Pulmonary vena-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)

1". Persistent pulmonary hypertension of the newborn (PPHN)

The diagnosis of WHO Group 1 PAH requires a right heart catheterization to demonstrate an mPAP ≥ 20mmHg at rest and a pulmonary vascular resistance (PVR) ≥ 3 Wood units, mean pulmonary capillary wedge pressure ≤ 15mmHg (to exclude pulmonary hypertension due to left heart disease, i.e., WHO Group 2 pulmonary hypertension) (4-6).

WHO Group 2: Pulmonary Hypertension Owing to Left Heart Disease

2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3: Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia

3.1 Chronic obstructive pulmonary disease
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 abnormalities

WHO Group 4: Chronic Thromboembolic Pulmonary Hypertension <CTEPHl

WHO Group 5: Pulmonary Hypertension with Unclear Multifactorial Mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher's disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

The American College of Chest Physicians (ACCP) has published an updated clinical practice guidelines for treating PAH (2). These guidelines use the New York Heart Association (NYHA)

functional classification of physical activity scale to classify PAH patients in classes I-IV based on the severity of their symptoms (3). Tyvaso is indicated for PAH patients with NYHA Functional Class III symptoms (1).

Class I	Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.
Class II	Patients with pulmonary hypertension resulting in slight limitation of physical activity. These patients are comfortable at rest, but ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class III	Patients with pulmonary hypertension resulting in marked limitation of physical activity. These patients are comfortable at rest, but less than ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class IV	Patients with pulmonary hypertension resulting in inability to perform any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may be present at rest, and discomfort is increased by any physical activity.

(3)

Regulatory Status

FDA-approved indications: Tyvaso is a prostacyclin mimetic indicated for the treatment of: (1)

- Pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability. Studies establishing effectiveness predominantly included patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%).
- Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability. The study establishing effectiveness predominately included patients with etiologies of 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%).

Tyvaso is a pulmonary and systemic vasodilator, concomitant administration of Tyvaso with diuretics, antihypertensive agents or other vasodilators may increase the risk of symptomatic hypotension. In patients with low systemic arterial pressure, Tyvaso may cause symptomatic hypotension (1).

Tyvaso inhibits platelet aggregation so there may be an increased risk of bleeding, particularly in patients receiving anticoagulants (1).

Tyvaso may cause acute bronchospasm. Patients with asthma or chronic obstructive pulmonary disease (COPD), or other bronchial hyperreactivity, are at increased risk for bronchospasm.

Patients should be optimally treated for reactive airway disease prior to and during treatment with Tyvaso (1).

Safety and effectiveness in pediatric patients less than 18 years of age have not been established (1).

Related policies
Adcirca, Adempas, Flolan/Veletri, Letairis, Opsumit, Opsynvi, Orenitram, PDE5 Inhibitor powders, Remodulin, Revatio, Tracleer, Uptravi, Ventavis, Winrevair

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Tyvaso may be considered **medically necessary** if the conditions indicated below are met.

Tyvaso may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Pulmonary Arterial Hypertension (PAH) - **WHO Group 1**
   a. NYHA functional classification of physical activity - **Class III**
2. Pulmonary Hypertension associated with interstitial lung disease (PH-ILD) – **WHO Group 3**

AND ALL of the following for **ALL** diagnoses:

a. Patients on antiplatelets or anticoagulants **only**: prescriber agrees to monitor patient for signs and symptoms of bleeding
b. Prescribed by or recommended by a cardiologist or pulmonologist

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Pulmonary Arterial Hypertension (PAH) – **WHO Group 1**
2. Pulmonary Hypertension associated with interstitial lung disease (PH-ILD) – **WHO Group 3**

AND ALL of the following for **ALL** diagnoses:

a. Symptoms have improved or stabilized
b. Patients on antiplatelets or anticoagulants **only**: prescriber agrees to monitor patient for signs and symptoms of bleeding

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Duration 2 years

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Tyvaso (treprostinil) is a prostacyclin analogue. Tyvaso's major pharmaceutical actions are direct vasodilation of pulmonary and systemic arterial vascular beds and inhibition of platelet aggregation. Tyvaso is indicated for the treatment of pulmonary hypertension. Safety and effectiveness of Tyvaso in patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Tyvaso while maintaining optimal therapeutic outcomes.

References

1. Tyvaso [package insert]. Research Triangle Park, NC: United Therapeutic Corp.; May 2022.
2. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll* Cardiol. 2013; 62:034-841. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll* Cardiol. 2013; 62:034-841.
3. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest.* 2014; 46(2):449-475.
4. Simonneau G, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53(1) Epub 2019 Jan 24.
5. Rose-Jones LJ and Mclaughlin V. Pulmonary Hypertension: Types and Treatments. Curr Cardiol Rev. 2015 Feb; 11(1): 73–79.
6. Rudolf KF, et al. Usefulness of pulmonary capillary wedge pressure as a correlate of left ventricular filling pressures in pulmonary arterial hypertension. The Journal of Heart and Lung Transplantation, Vol33, No2. February 2014.

Policy History

Date	Action	Reason
May 2012	Updated the NYHA indication to only Class III symptoms.	
March 2013	Annual editorial review and reference update	
March 2014	Annual review	
March 2015	Annual editorial review and reference update. Addition of age 18	
June 2016	Annual editorial review and reference update. Updated PAH classifications Policy number change from 5.06.08 to 5.40.13	
September 2017	Annual editorial review and reference update	
September 2018	Annual review and reference update	
September 2019	Annual editorial review. Changed approval duration from lifetime to 2 years	
March 2020	Annual review. Revised background section and added requirement for patients on antiplatelets or anticoagulants to be monitored for bleeding. Also added initial requirement of prescribed by or recommended by a cardiologist or pulmonologist per SME	
April 2021	Addition of indication: pulmonary hypertension associated with ILD (PH-ILD; WHO Group 3)	
June 2021	Annual review	
December 2021	Annual review	

September 2022	Annual review and reference update. Per SME, added bronchospasm warning to regulatory status section
December 2022	Annual review
September 2023	Annual review
March 2024	Annual review
September 2024	Annual review
March 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.