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# 5.40.012

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	October 1, 2024
<b>Subsection:</b>	Cardiovascular Agents	<b>Original Policy Date:</b>	June 9, 2011
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**Last Review Date:** September 6, 2024

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## Ventavis

### Description

#### Ventavis (iloprost)

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#### Background

Pulmonary arterial hypertension is a rare disorder of the pulmonary arteries in which the pulmonary arterial pressure rises above normal levels in the absence of left ventricular failure. This condition can progress to cause right-sided heart failure and death (1). Ventavis is indicated for treatment of pulmonary arterial hypertension (PAH) which is classified by WHO as Group 1. Ventavis is used to treat pulmonary arterial hypertension (PAH, high blood pressure in the lungs) to improve exercise ability (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

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- 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  $\geq$  20mmHg at rest and a pulmonary vascular resistance (PVR)  $\geq$  3 Wood units, mean pulmonary capillary wedge pressure  $\leq$  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 <CTEPH**

### **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

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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 guideline for treating PAH. 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).

Ventavis is indicated for patients with NYHA Functional Class III or IV (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: Ventavis is a synthetic analog of prostacyclin indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration. Studies establishing effectiveness included predominately patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH (65%) or PAH associated with connective tissue diseases (23%) (1).

Hypotension leading to syncope has been reported with Ventavis. When treatment is started, vital signs need to be monitored. Iloprost should not be administered to patients with systolic blood pressure less than 85 mm Hg (1).

Ventavis therapy should be stopped in the presence of pulmonary edema. Ventavis inhalation can induce bronchospasm. Bronchospasm may be more severe or frequent in patients with a history of hyper-reactive airways. Ventavis has not been evaluated in patients with chronic obstructive pulmonary disease (COPD), severe asthma, or with acute pulmonary infections (1).

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Since Ventavis inhibits platelet function, there is a potential for increased risk of bleeding, particularly in patients maintained on anticoagulants or platelet inhibitors (1).

Iloprost is in pregnancy category C. There are no adequate and well controlled studies in pregnant women. Ventavis should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Safety and efficacy in pediatric patients have not been established (1).

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### Related policies

Adcirca, Adempas, Flolan/Veletri, Letairis, Opsumit, Opsynvi, Orenitram, PDE5 Inhibitor powders, Remodulin, Revatio, Tracleer, Tyvaso, Upravi, 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.*

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

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

## Prior-Approval Requirements

**Age** 18 years of age or older

### Diagnoses

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

1. Pulmonary Arterial Hypertension (PAH) – **WHO Group I**
2. NYHA functional classification of physical activity - **Class III or IV**
3. Systolic blood pressure greater than or equal to 85 mm Hg
4. Prescriber agrees to monitor patient for signs and symptoms of pulmonary edema and discontinue if confirmed
5. Patients on antiplatelets or anticoagulants **only**: prescriber agrees to monitor patient for signs and symptoms of bleeding
6. Prescribed by or recommended by a cardiologist or pulmonologist

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## Prior – Approval *Renewal* Requirements

**Age** 18 years of age or older

### Diagnoses

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

1. Pulmonary Arterial Hypertension (PAH) – **WHO Group I**
2. Symptoms have improved or stabilized
3. Systolic blood pressure greater than or equal to 85 mm Hg
4. Prescriber agrees to monitor patient for signs and symptoms of pulmonary edema and discontinue if confirmed
5. 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

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## Prior – Approval *Renewal* Limits

Same as above

### Rationale

#### Summary

Pulmonary arterial hypertension is a rare disorder of the pulmonary arteries in which the pulmonary arterial pressure rises above normal levels in the absence of left ventricular failure. This condition can progress to cause right-sided heart failure and death (1). The FDA has

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approved Ventavis (iloprost), a synthetic analog of prostacyclin, for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) in patients with NYHA class III or IV symptoms (2). Hypotension leading to syncope has been reported with Ventavis. Safety and efficacy in pediatric patients have not been established (1).

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

## References

1. Ventavis [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; March 2022.
2. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013; 62:034-841.
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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
March 2013	Annual editorial review and reference update
March 2014	Annual review and reference update
March 2015	Annual review and reference update, Addition of age 18
June 2016	Annual editorial review and reference update Updated PAH classifications Addition of prescriber agrees to monitor patient for signs and symptoms of pulmonary edema and discontinue if confirmed Policy number change from 5.06.09 to 5.40.12
September 2017	Annual editorial review
September 2018	Annual review and reference update
September 2019	Annual editorial review. Changed approval duration from lifetime to 2 years
March 2020	Annual review and reference update. Revised background section and added requirement for patients on antiplatelets or anticoagulants to be

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	monitored for bleeding. Also added initial requirement of prescribed by or recommended by a cardiologist or pulmonologist per SME
December 2021	Annual review and reference update
September 2022	Annual review and reference update
December 2022	Annual review
September 2023	Annual review
March 2024	Annual review
September 2024	Annual review

## [Keywords](#)

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**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.**