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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Cardiovascular Agents	**Original Policy Date:**	January 15, 2016
Subject:	Uptravi	**Page:**	1 of 7

Last Review Date: March 8, 2024

Uptravi

Description

Uptravi (selexipag) tablets

*Uptravi IV is for hospital use only and this policy does not apply

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 (1-2), Uptravi is indicated for treatment of pulmonary arterial hypertension (PAH) which is classified by WHO as Group 1. Uptravi 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
- 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 <CTEPHI

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 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. Uptravi is indicated for patients with NYHA Functional Class III symptoms (3).

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 indication: Uptravi is a prostacyclin receptor agonist indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH. Effectiveness was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms (1).

Uptravi should be discontinued if signs or symptoms of pulmonary edema occur (1).

Concomitant use with strong CYP2C8 inhibitors is contraindicated (1).

For patients who do not have a positive acute vasodilator testing and are considered lower risk based on clinical assessment, oral therapy with endothelin receptor antagonist (ERA) or phosphodiesterase type 5 inhibitor (PDE-5I) would be the first line of therapy recommended (4).

Safety and efficacy in pediatric patients have not been established (1).

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

Policy

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

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

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

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Pulmonary Arterial Hypertension – **WHO Group I**

AND ALL of the following:

1. NYHA functional classification of physical activity - **Class II-III**
2. Prescriber agrees to monitor patient for signs and symptoms of pulmonary edema and discontinue if confirmed
3. Inadequate treatment response, intolerance, or contraindication to endothelin receptor antagonist (ERA) or phosphodiesterase type 5 inhibitor (PDE-5I)
4. Prescribed by or recommended by a cardiologist or pulmonologist

AND NONE of the following:

1. Severe hepatic impairment (Child-Pugh Class C)

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Pulmonary Arterial Hypertension – **WHO Group I**

AND ALL of the following:

1. Symptoms have improved or stabilized
2. Prescriber agrees to monitor patient for signs and symptoms of pulmonary edema and discontinue if confirmed

AND NONE of the following:

1. Severe hepatic impairment (Child-Pugh Class C)

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Quantity

Initiation / Titration	Uptravi 200-800mcg dosepak
	Uptravi 200mcg tablet
Maintenance Therapy	180 tablets per 90 days
	Maximum daily dose of 3200mcg

Duration 2 years

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. Uptravi is a prostacyclin vasodilator indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) in patients with NYHA class II-III symptoms (1).

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

References

1. Uptravi [package insert]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.; July 2022.
2. 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
January 2016	Addition to PA	
March 2016	Annual review	
June 2016	Annual editorial review Addition of the Initiation / Titration: Uptravi 200-800mcg dosepak and Uptravi 200mcg tablet and no severe hepatic impairment (Child-Pugh Class C)	
November 2016	Addition of inadequate treatment response, intolerance, or contraindication to endothelin receptor antagonist (ERA) or phosphodiesterase type 5 inhibitor	
March 2017	Annual review	
September 2017	Annual 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 initial requirement of prescribed by or recommended by a cardiologist or pulmonologist per SME	
August 2021	Added statement that Uptravi IV is for hospital use only and this policy does not apply	
December 2021	Annual review	
September 2022	Annual review and reference update	
December 2022	Annual review	

September 2023	Annual review and reference update
March 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.