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Section:	Prescription Drugs	**Effective Date:**	October 1, 2024
Subsection:	Cardiovascular Agents	**Original Policy Date:**	January 1, 2014
Subject:	Opsumit	**Page:**	1 of 7

Last Review Date: September 6, 2024

Opsumit

Description

Opsumit (macitentan)

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. Opsumit is indicated for treatment of pulmonary arterial hypertension (PAH) which is classified by WHO as Group 1. Opsumit 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 <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. 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). Opsumit is indicated for patients with NYHA Functional Class II and III (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 indication: Opsumit is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and hospitalization for PAH. Disease progression included: death, initiation of intravenous (IV) or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms and need for additional PAH treatment) (1).

Opsumit contains a boxed warning for embryo-fetal toxicity. Females of childbearing potential should have pregnancy excluded before the start of treatment with Opsumit, prevented during therapy, and for one month after treatment cessation. All female patients must take part in the Opsumit Risk Evaluation and Mitigation Strategy (REMS) (1).

Hepatotoxicity has occurred with Opsumit use. Patients should have a baseline liver function test and be monitored periodically for liver enzyme and signs and symptoms failure. Additionally, there have been post-administration reports of decreases in hemoglobin

concentration and hematocrit that have resulted in anemia. It is recommended that hemoglobin concentrations be checked after 1 and 3 months, and every 3 months thereafter. Should signs of pulmonary edema occur, consider the possibility of associated pulmonary veno-occlusive disease and consider whether Opsumit should be discontinued (1).

The recommended dosage of Opsumit is 10 mg once daily for oral administration. Doses higher than 10 mg once daily have not been studied in patients with PAH and are not recommended (1).

The safety and efficacy of Opsumit in children have not been established (1).

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

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

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

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Pulmonary Arterial Hypertension (PAH) - **WHO Group I**
    a. NYHA functional **class II or III**

AND ALL of the following:

1. For females only, regardless of reproductive potential, the patient and prescriber are enrolled in the Opsumit REMS program

2. Absence of clinically significant anemia
3. Prescribed by or recommended by a cardiologist or pulmonologist
4. Females of reproductive potential **only**: patient should have pregnancy excluded before the start of treatment with Opsumit and patient should be advised to use effective contraception during treatment and for one month after the last dose
5. Prescriber agrees to monitor for pulmonary edema and discontinue if confirmed

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Pulmonary Arterial Hypertension (PAH) - **WHO Group I**

AND ALL of the following:

1. Symptoms have improved or stabilized
2. Females of reproductive potential **only**: patient should be advised to use effective contraception during treatment with Opsumit and for one month after the last dose
3. Prescriber agrees to monitor for pulmonary edema and discontinue if confirmed

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 90 tablets per 90 days

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. Opsumit is an endothelin receptor antagonist indicated for treatment of pulmonary arterial hypertension (WHO Group I) in patients with NYHA class II or III to improve exercise ability and to decrease clinical worsening (1).

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

References

1. Opsumit [package insert]. Titusville, NJ: Actelion Pharmaceuticals US, Inc; March 2024.
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
December 2013	New Addition to PA
March 2014	Annual review
March 2015	Annual review and reference update
June 2016	Annual editorial review and reference update

	Addition of age 18 and the prescriber agrees to monitor for pulmonary edema and discontinue therapy if confirmed Policy number change from 5.06.20 to 5.40.20
September 2017	Annual editorial review and reference update
September 2018	Annual review
September 2019	Annual editorial review and reference update. Changed approval duration from lifetime to 2 years
March 2020	Annual review. Revised background section and added initiation requirement of no clinically significant anemia. Also added initial requirement of prescribed by or recommended by a cardiologist or pulmonologist per SME
September 2021	Annual review and reference update
December 2021	Annual review
September 2022	Annual editorial review and reference update. Updated contraception requirement for consistency
December 2022	Annual review
September 2023	Annual review and reference update
March 2024	Annual review
September 2024	Annual editorial review and reference update

Keywords

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