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
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
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).

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>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.</td>
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<tr>
<td>Class II</td>
<td>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.</td>
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<tr>
<td>Class III</td>
<td>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.</td>
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<tr>
<td>Class IV</td>
<td>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</td>
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</tbody>
</table>

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. 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). Opsumit also reduced hospitalization for PAH (1).

Opsumit is a pregnancy category X medication. 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, Remodulin, Revatio, Tracleer, Tyvaso, Uptravi, 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.

Opsumit may be considered medically necessary for treatment of patients 18 years of age and older with pulmonary arterial hypertension, WHO Group I and if the conditions indicated below are met.

Opsumit may be considered investigational for patients less than 18 years of age and 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. 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.
3. 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 childbearing potential should have pregnancy excluded before the start of treatment with Opsumit, prevented during therapy and for one month after treatment cessation
   3. Prescriber agrees to monitor for pulmonary edema and discontinue if confirmed

### Policy Guidelines

**Pre - PA Allowance**

None

**Prior - Approval Limits**

<table>
<thead>
<tr>
<th>Quantity</th>
<th>90 tablets per 90 days</th>
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<tbody>
<tr>
<td>Duration</td>
<td>2 years</td>
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</table>

**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

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td>December 2013</td>
<td>New Addition to PA</td>
</tr>
<tr>
<td>March 2014</td>
<td>Annual review</td>
</tr>
<tr>
<td>March 2015</td>
<td>Annual review and reference update</td>
</tr>
<tr>
<td>June 2016</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td></td>
<td>Addition of age 18 and the prescriber agrees to monitor for pulmonary edema and discontinue therapy if confirmed</td>
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<tr>
<td></td>
<td>Policy number change from 5.06.20 to 5.40.20</td>
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<tr>
<td>September 2017</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>September 2018</td>
<td>Annual review</td>
</tr>
<tr>
<td>September 2019</td>
<td>Annual editorial review and reference update. Changed approval duration from lifetime to 2 years</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on
September 13, 2019 and is effective on October 1, 2019.