## Uptravi

### Description

Uptravi (selexipag)

### 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
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).

<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: 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, 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 for treatment of patients 18 years of age or older with pulmonary arterial hypertension (PAH) and if the conditions indicated below are met.

Uptravi may be considered investigational in patients under the age of 18 and for all other diagnoses and functional classes.

**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)

**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**

February 2019.

### Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Reason</th>
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<tbody>
<tr>
<td>January 2016</td>
<td>Addition to PA</td>
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<tr>
<td>March 2016</td>
<td>Annual review</td>
<td></td>
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<tr>
<td>June 2016</td>
<td>Annual editorial review</td>
<td></td>
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<tr>
<td>November 2016</td>
<td>Addition of the Initiation / Titration: Uptravi 200-800mcg dosepak and Uptravi 200mcg tablet and no severe hepatic impairment (Child-Pugh Class C)</td>
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<tr>
<td>March 2017</td>
<td>Annual review</td>
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<tr>
<td>September 2017</td>
<td>Annual review</td>
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<tr>
<td>September 2018</td>
<td>Annual review and reference update</td>
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<tr>
<td>September 2019</td>
<td>Annual editorial review</td>
<td>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.