EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

# Uptravi

*selexipag*

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AUTHORISED
This medicine is authorised for use in the European Union.

## Overview

This is a summary of the European public assessment report (EPAR) for Uptravi. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Uptravi.

For practical information about using Uptravi, patients should read the package leaflet or contact their doctor or pharmacist.

## What is Uptravi and what is it used for?

Uptravi is a medicine used to treat adults with pulmonary arterial hypertension (PAH, abnormally high blood pressure in the arteries of the lungs). It can be used in combination with other medicines called endothelin receptor antagonists (ERA) or phosphodiesterase type-5 (PDE-5) inhibitors or on its own for patients for whom these medicines are not suitable. Uptravi is used in patients with functional class II or III PAH. The 'class' reflects the severity of the disease: 'class II' involves slight limitation of physical activity while 'class III' involves marked limitation of physical activity.

Uptravi contains the active substance selexipag.

## How is Uptravi used?

Uptravi can only be obtained with a prescription and treatment should only be started and monitored by a doctor who has experience in the treatment of PAH.

Uptravi is available as tablets (200; 400; 600; 800; 1,000; 1,200; 1,400 and 1,600 micrograms). Treatment should be started at a dose of 200 micrograms twice a day, approximately 12 hours apart. The dose is then increased weekly, as long as it is tolerated, to a maximum of 1,600 micrograms twice daily, which is then continued afterwards. Patients may tolerate treatment better if they take their tablets with food and take the first tablet of an increased dose in the evening rather than the morning. If the patient cannot tolerate an increased dose, the doctor may have to reduce it.

If stopping treatment with Uptravi, the dose should be reduced gradually.

Patients with severely reduced liver function should not take Uptravi. Patients with moderately reduced liver function should start with 200 micrograms once daily. If tolerated, this dose can be increased weekly. For further information, see the package leaflet.

## How does Uptravi work?

PAH is a debilitating disease where there is severe narrowing of the blood vessels of the lungs. This leads to high blood pressure in the vessels taking blood from the heart to the lungs and reduces the amount of oxygen that can get into the blood in the lungs, making physical activity more difficult.

The active substance in Uptravi, selexipag, is a 'prostacyclin receptor agonist'. This means that it works in a similar way to prostacyclin, a naturally occurring substance that regulates blood pressure by attaching to receptors in the muscles of blood vessel walls, causing the vessels to relax and widen. By attaching to prostacyclin receptors, Uptravi also widens the blood vessels and so lowers the pressure inside them, improving symptoms of the disease.

## What benefits of Uptravi have been shown in studies?

The benefits of Uptravi for PAH were shown in one main study involving 1,156 patients with PAH. Patients were given either Uptravi or placebo (a dummy treatment) for around 70 weeks. Patients were either previously untreated or receiving treatment with other PAH medicines (ERA or PDE-5 inhibitors). The main measure of effectiveness was based on the number of patients whose disease worsened or who died during treatment or shortly after treatment had ended. Overall, 24.4% (140 out of 574) of patients treated with Uptravi either died or showed signs of worsening disease compared with 36.4% (212 out of 582) of patients treated with placebo.

## What are the risks associated with Uptravi?

The most common side effects with Uptravi (which may affect more than 1 in 10 people) are headache, diarrhoea, nausea and vomiting, jaw pain, myalgia (muscle pain), pain in the limbs, arthralgia (joint pain) and

flushing. These effects are mild or moderate and are most frequently seen while the dose of Uptravi is being increased.

Uptravi must not be used in patients who have had a heart attack within the last 6 months, severe coronary heart disease (heart disease caused by the obstruction of the blood vessels that supply the heart muscle) or unstable angina (a severe type of chest pain). It must not be used in patients with severe arrhythmias (unstable heartbeat) or defects in the heart valves. For patients with other heart problems, Uptravi must only be used under close medical supervision. It must also not be used in patients who have had a stroke within the last 3 months. Uptravi must not be taken at the same time as medicines, such as gemfibrozil, that are strong blockers (inhibitors) of the liver enzyme CYP2C8.

For the full list of restrictions and side effects reported with Uptravi, see the package leaflet.

## Why is Uptravi approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Uptravi's benefits are greater than its risks and recommended that it be approved for use in the EU. Patients with PAH currently have very limited treatment options; therefore there is a high unmet medical need. Uptravi has been shown to be more effective than placebo at preventing worsening of PAH, on its own and when used in addition to an ERA and/or a PDE-5 inhibitor. Compared with other medicines in the same class which are given into a vein, Uptravi has the advantage of being given by mouth. Regarding safety, the side effects with Uptravi are considered acceptable. Although the CHMP noted a small apparent increase in the rate of death for patients taking Uptravi when compared with placebo, they considered that this was due to chance or to the way the study was designed and therefore did not impact the benefits or risks of the medicine.

## What measures are being taken to ensure the safe and effective use of Uptravi?

Any prescriber of Uptravi will have to register first with the company that markets Uptravi before being able to prescribe it. The company will provide educational materials for the healthcare professionals who will prescribe

and dispense the medicine to help them prescribe the medicine correctly and avoid medication errors. These materials will also include a guide and diary to be given to patients to help them keep track of the number of tablets to take and explain how doses should be increased. The diary contains boxes for the patient to mark the number and strength of tablets they take each day.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Uptravi have also been included in the summary of product characteristics and the package leaflet.

## Other information about Uptravi

The European Commission granted a marketing authorisation valid throughout the European Union for Uptravi on 12 May 2016.

For more information about treatment with Uptravi, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

Uptravi : EPAR - Summary for the public (PDF/86.9 KB)

First published: 26/05/2016
Last updated: 19/07/2017

Available languages (22)

Uptravi : EPAR - Risk-management-plan summary (PDF/123.73 KB)

First published: 11/02/2021
Last updated: 11/02/2021

More detail is available in the summary of product characteristics

This EPAR was last updated on 23/03/2021

## Authorisation details

| Product details | |
|---|---|
| Name | Uptravi |
| Agency product number | EMEA/H/C/003774 |
| Active substance | Selexipag |
| International non-proprietary name (INN) or common name | selexipag |
| Therapeutic area (MeSH) | Hypertension, Pulmonary |
| Anatomical therapeutic chemical (ATC) code | B01AC27 |

| Publication details | |
|---|---|
| Marketing-authorisation holder | Janssen Cilag International NV |
| Revision | 12 |
| Date of issue of marketing authorisation valid throughout the European Union | 12/05/2016 |

## Publication details

| | |
|---|---|
| Contact address | Turnhoutseweg 30<br>B 2340 Beerse<br>Belgium |

# Product information

09/03/2021 Uptravi - EMEA/H/C/003774 - IA/0033

Uptravi : EPAR - Product Information (PDF/1.79 MB)

First published: 26/05/2016
Last updated: 23/03/2021

Available languages (24)

### Contents


- Annex I - Summary of product characteristics
- Annex IIA - Manufacturing-authorisation holder responsible for batch release
- Annex IIB - Conditions of the marketing authorisation
- Annex IIIA - Labelling
- Annex IIIB - Package leaflet


Please note that the size of the above document can exceed 50 pages.

You are therefore advised to be selective about which sections or pages you wish to print.

Uptravi : EPAR - All Authorised presentations (PDF/29.76 KB)

First published: 26/05/2016
Last updated: 07/02/2017

Available languages (24)

**Pharmacotherapeutic group**

Antithrombotic agents

**Therapeutic indication**

Uptravi is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO functional class (FC) II–III, either as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type 5 (PDE-5) inhibitor, or as monotherapy in patients who are not candidates for these therapies.

Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

## Assessment history

**Changes since initial authorisation of medicine**

Uptravi : EPAR - Procedural steps taken and scientific information after authorisation (PDF/205.21 KB)

First published: 26/10/2016
Last updated: 23/03/2021

CHMP post-authorisation summary of positive opinion for Uptravi (II-07) (PDF/74.83 KB)

Adopted

First published: 19/05/2017
EMA/CHMP/315335/2017

## Initial marketing-authorisation documents

Uptravi : EPAR - Public assessment report (PDF/5.22 MB)

Adopted

First published: 26/05/2016
Last updated: 26/05/2016
EMA/272184/2016

CHMP summary of opinion for Uptravi (PDF/107.37 KB)

Adopted

First published: 29/01/2016
Last updated: 01/04/2016
EMA/CHMP/826224/2015

## News

- Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 15-18 May 2017
  19/05/2017
- Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 3-6 April 2017
  07/04/2017
- EMA concludes safety review of Uptravi
  07/04/2017
- EMA reviewing safety of Uptravi for pulmonary arterial hypertension (updated)*
  14/02/2017
- Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 6-9 February 2017
  10/02/2017
- Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 29 March - 1 April 2016
  01/04/2016
- Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 25-28 January 2016
  29/01/2016

## Preventing medication errors

Uptravi: educational brochure for healthcare professionals and diary for patients (PDF/353.84 KB)

First published: 31/05/2016
Last updated: 31/05/2016
EMA/89167/2016

Available languages (22)

## More information on Uptravi

This product is no longer an orphan medicine. It was originally designated an orphan medicine on 26 August 2005. Uptravi was withdrawn from the Community register of orphan medicinal products in February 2016, upon request of the marketing authorisation holder at the time of the granting of a marketing authorisation.

## Related content

- Uptravi: Paediatric investigation plan


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