Package leaflet: Information for the patient

Uptravi 200 microgram film-coated tablets
Uptravi 400 microgram film-coated tablets
Uptravi 600 microgram film-coated tablets
Uptravi 800 microgram film-coated tablets
Uptravi 1,000 microgram film-coated tablets
Uptravi 1,200 microgram film-coated tablets
Uptravi 1,400 microgram film-coated tablets
Uptravi 1,600 microgram film-coated tablets
Selexipag

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you have any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet (see section 4).

What is in this leaflet

1. What Uptravi is and what it is used for

Uptravi is a medicine that contains the active substance selexipag. It acts on blood vessels in a similar way to the natural substance prostacyclin, making them relax and widen.

Uptravi is used for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients insufficiently controlled with other types of medicines for PAH known as endothelin receptor antagonists and phosphodiesterase type 5 inhibitors. Uptravi can be used on its own if the patient is not a candidate for these medicines.

PAH is high blood pressure in the blood vessels that carry blood from the heart to the lungs (the pulmonary arteries). In people with PAH, these arteries narrow, so the heart has to work harder to pump blood through them. This may cause people to feel tired, dizzy, short of breath, or experience other symptoms.

By mimicking the action of prostacyclin, Uptravi widens the pulmonary arteries and reduces their hardening. This makes it easier for the heart to pump blood through the pulmonary arteries. It relieves the symptoms of PAH and improves the course of the disease.

2. What you need to know before you take Uptravi

Do not take Uptravi

- if you are allergic to selexipag or any of the other ingredients of this medicine (listed in section 6).
- if you have a heart problem, such as:
  - poor blood flow to the heart muscles (severe coronary heart disease or unstable angina); symptoms can include chest pain
  - heart attack within the last 6 months
  - weak heart (decompensated cardiac failure) that is not under close medical observation
  - severe irregular heartbeat
  - defect of the heart valves (inborn or acquired) that causes the heart to work poorly (not related to pulmonary hypertension)
- if you have had a stroke within the last 3 months, or any other occurrence that reduced the blood supply to the brain (e.g., transient ischaemic attack)
- if you are taking gemfibrozil (medicine used to lower the level of fats [lipids] in the blood)

Warnings and precautions

Talk to your PAH doctor or nurse before taking Uptravi if you
- are taking medicines for high blood pressure
- have low blood pressure associated with symptoms such as dizziness
- have recently experienced significant blood loss or fluid loss such as severe diarrhoea or vomiting
- have problems with your thyroid gland
- have severe problems with your kidneys or are undergoing dialysis
- have or have had severe problems with your liver not working properly
- are taking clopidogrel, deferasirox, or teriflunomide

If you notice any of the above signs or your condition changes, **tell your doctor immediately**.

Children and adolescents

Do not give this medicine to children under 18 years of age, because Uptravi has not been tested in children.

Elderly patients

There is limited experience with Uptravi in patients older than 75 years. Uptravi should be used with caution in this age group.

Other medicines and Uptravi

Tell your doctor if you are taking, have recently taken, or might take any other medicines.
Taking other medicines may affect how Uptravi works.

Talk to your PAH doctor or nurse if you are taking any of the following medicines:
- Gemfibrozil (medicine used to lower the level of fats [lipids] in the blood)
- Clopidogrel (medicine used to inhibit blood clots in coronary artery disease)
- Deferasirox (medicine used to remove iron from the blood stream)
- Teriflunomide (medicine used to treat relapsing-remitting multiple sclerosis)
- Carbamazepine (medicine used to treat some forms of epilepsy, nerve pain or to help control serious mood disorders when some other medicines do not work)
- Phenytoin (medicine used to treat epilepsy)
- Valproic acid (medicine used to treat epilepsy)
- Probenecid (medicine used to treat gout)
- Fluconazole, rifampicin or rifapentine (antibiotics used to treat infections)

Pregnancy and breast-feeding

Uptravi is not recommended during pregnancy and breast-feeding. If you are a woman who can have children, you should use an effective contraceptive method while taking Uptravi. If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before taking this medicine.

Driving and using machines

Uptravi can cause side effects such as headaches and low blood pressure (see section 4), which may affect your ability to drive; the symptoms of your condition can also make you less fit to drive.

3. How to take Uptravi

Uptravi should only be prescribed by a doctor experienced in the treatment of PAH. Always take Uptravi exactly as your doctor has told you. Check with your doctor if you are not sure or have any questions.

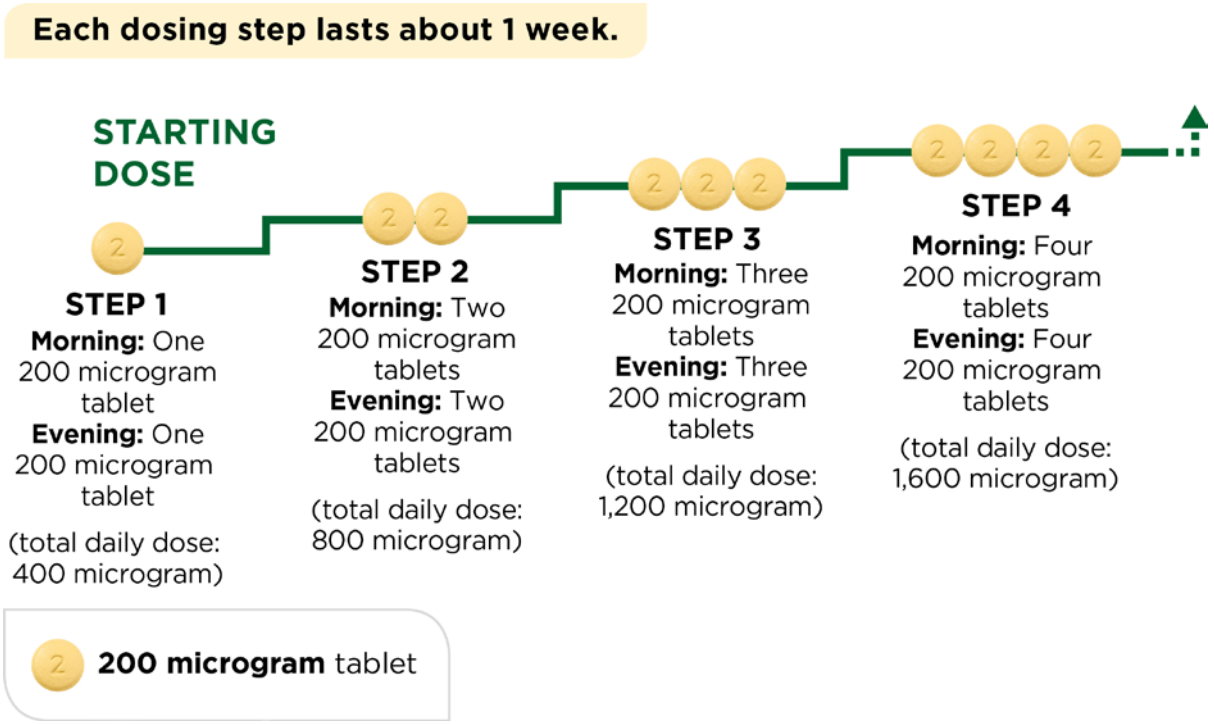
If you have poor vision or experience any type of blindness, get help from another person when taking Uptravi during the titration period.

Finding the right dose for you

At the start of treatment, you will take the lowest dose. This is one 200 microgram tablet **in the morning and another 200 microgram tablet in the evening**. Treatment should be initiated in the evening. Your doctor will instruct you to gradually increase your dose. This is called titration. It lets your body adjust to the new medicine. The goal of titration is to reach the most appropriate dose. This will be the highest dose you can tolerate, which may reach the maximum dose of 1,600 micrograms in the morning and in the evening.

The first pack of tablets you receive will contain the light-yellow 200 microgram tablets.
Your doctor will tell you to increase your dose in steps, usually every week but the interval between increases could be longer.

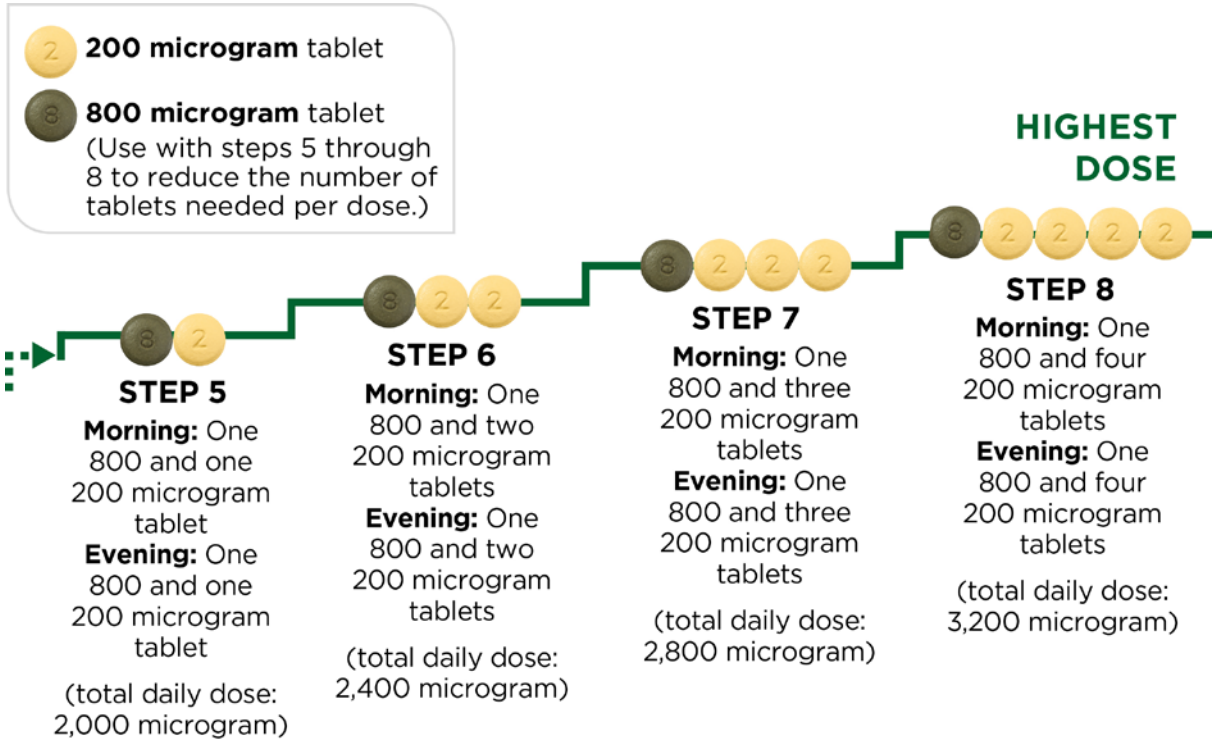
With each step, you will add one 200 microgram tablet to your morning dose and another 200 microgram tablet to your evening dose. The first intake of the increased dose should be in the evening. The diagram below shows the number of tablets to take **every morning** and **every evening** for the first 4 steps.



If your doctor instructs you to further increase your dose and move to step 5, this may be done by taking one green 800 microgram tablet and one light-yellow 200 microgram tablet in the morning and one 800 microgram tablet and one 200 microgram tablet in the evening.

If your doctor tells you to increase your dose further, you will add one 200 microgram tablet to your morning dose and one 200 microgram tablet to your evening dose with each new step. The first intake of the increased dose should be in the evening. The maximum dose of Uptravi is 1,600 micrograms in the morning and 1,600 micrograms in the evening. However, not every patient will reach this dose, because different patients require different doses.

The diagram below shows the number of tablets to take **every morning** and **every evening** at each step, starting with step 5.



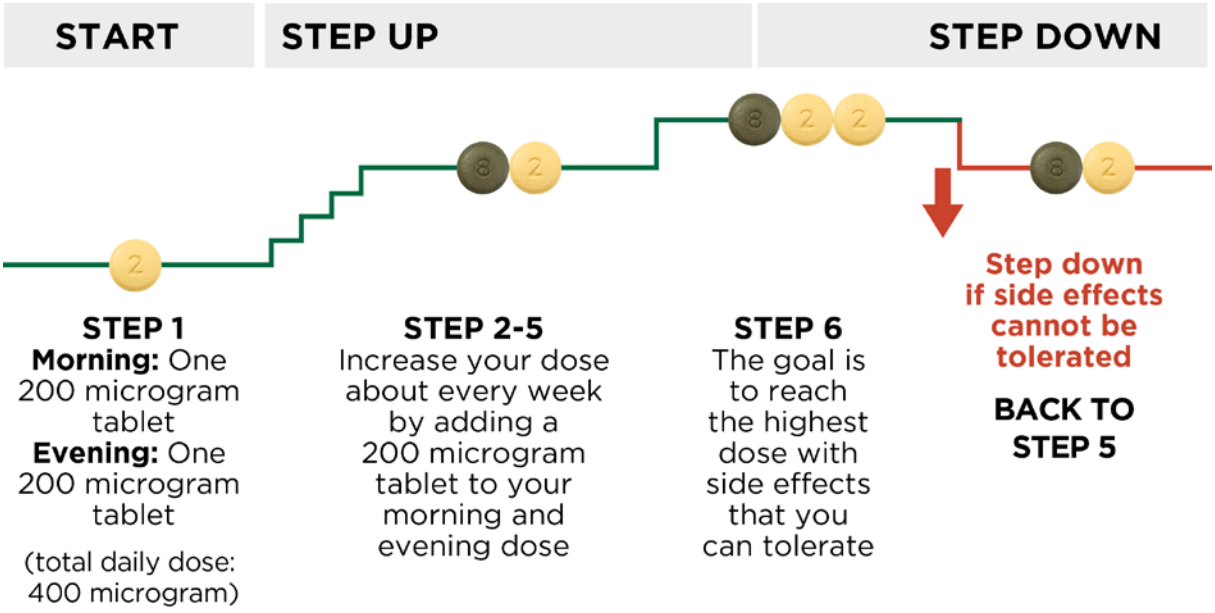
The titration pack also contains a titration guide providing information on the titration process and allowing you to record the number of tablets you take every day.

Remember to record the number of tablets you take every day in your titration diary. The titration steps usually last about 1 week. If your doctor instructs you to prolong each titration step longer than 1 week, there are additional diary pages to allow you to track this. **Remember to talk to your PAH doctor or nurse regularly during titration.**

Stepping down to a lower dose due to side effects

During titration, you may experience side effects such as headache, diarrhoea, feeling sick (nausea), being sick (vomiting), jaw pain, muscle pain, leg pain, joint pain, or reddening of the face (see section 4). If these side effects are difficult for you to tolerate, talk to your doctor about how to manage or treat them. There are treatments available that can help relieve the side effects. For example, painkillers such as paracetamol may help treat pain and headache.

If the side effects cannot be treated or do not gradually get better on the dose you are taking, your doctor may adjust your dose by reducing the number of 200 microgram light-yellow tablets you take by one in the morning and by one in the evening. The diagram below shows stepping down to a lower dose. Do this only if instructed to do so by your doctor.



If your side effects are manageable after stepping down your dose, your doctor may decide that you should stay on that dose. Please see section Maintenance dose below for more information.

Maintenance dose

The highest dose that you can tolerate during titration will become your maintenance dose. Your maintenance dose is the dose you should continue to take on a regular basis.

Your doctor will prescribe a suitable tablet strength for your maintenance dose. **This allows you to take one tablet in the morning and one in the evening, instead of multiple tablets each time.**

For a full description of Uptravi tablets, including colours and marking, please see section 6 of this leaflet.

Over time, your doctor may adjust your maintenance dose as needed.

If, at any time, after taking the same dose for a long time, you experience side effects that you cannot tolerate or side effects that have an impact on your normal daily activities, contact your doctor as your dose may need to be reduced. The doctor may then prescribe you a lower single-tablet strength. Please remember to dispose of unused tablets (see section 5).

Take Uptravi once in the morning and once in the evening, about 12 hours apart.
Take the tablets with meals as you might tolerate your medicine better. Swallow the tablets whole with a glass of water. Do not split, crush or chew the tablets.

If you take more Uptravi than you should

If you have taken more tablets than you have been told to take, ask your doctor for advice.

If you forget to take Uptravi

If you forget to take Uptravi, take a dose as soon as you remember, then continue to take your tablets at the usual times. If it is nearly time for your next dose (within 6 hours before you would normally take it), you should skip the missed dose and continue to take your medicine at the usual time. Do not take a double dose to make up for a forgotten tablet.

If you stop taking Uptravi

Suddenly stopping your treatment with Uptravi might lead to your symptoms getting worse. Do not stop taking Uptravi unless your doctor tells you to. Your doctor may tell you to reduce the dose gradually before stopping completely.

If, for any reason, you stop taking Uptravi for more than 3 consecutive days (if you missed 3 morning and 3 evening doses, or 6 doses in a row or more), **contact your doctor immediately as your dose may need to be adjusted to avoid side effects**. Your doctor may decide to restart your treatment on a lower dose, gradually increasing to your previous maintenance dose.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, Uptravi can cause side effects. You may experience side effects not only during the titration period when your dose is being increased, but also later after taking the same dose for a long time.

If you experience any of these side effects: headache, diarrhoea, feeling sick (nausea), being sick (vomiting), jaw pain, muscle pain, leg pain, joint pain, or reddening of the face, that you cannot tolerate or that cannot be treated, you should contact your doctor as the dose you are taking maybe too high for you and may need to be reduced.

Very common side effects (may affect more than 1 in 10 people)
- Headache
- Flushing (reddening of the face)
- Nausea and vomiting (feeling sick and being sick)
- Diarrhoea
- Jaw pain, muscle pain, joint pain, leg pain
- Nasopharyngitis (stuffy nose)

Common side effects (may affect up to 1 in 10 people)
- Anaemia (low red blood cell levels)
- Hyperthyroidism (overactive thyroid gland)
- Decreased appetite
- Weight loss
- Hypotension (low blood pressure)
- Stomach pain
- Pain
- Changes in some blood test results including those measuring blood cell counts or your thyroid function
- Rashes, including hives, may cause a burning or stinging sensation and skin redness

Uncommon side effects (may affect up to 1 in 100 people)
- Increased heart rate

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

5. How to store Uptravi

Keep this medicine out of the sight and reach of children.

Do not use Uptravi after the expiry date, which is stated on the carton and on the blister after "EXP." The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

No special requirements for disposal.

6. Contents of the pack and other information

What Uptravi contains

- The active substance is selexipag.
  Uptravi 200 microgram film-coated tablets contain 200 micrograms of selexipag
  Uptravi 400 microgram film-coated tablets contain 400 micrograms of selexipag
  Uptravi 600 microgram film-coated tablets contain 600 micrograms of selexipag
  Uptravi 800 microgram film-coated tablets contain 800 micrograms of selexipag
  Uptravi 1,000 microgram film-coated tablets contain 1,000 micrograms of selexipag
  Uptravi 1,200 microgram film-coated tablets contain 1,200 micrograms of selexipag
  Uptravi 1,400 microgram film-coated tablets contain 1,400 micrograms of selexipag
  Uptravi 1,600 microgram film-coated tablets contain 1,600 micrograms of selexipag

- The other ingredients are:
  In the tablet core:
  Mannitol (E421), maize starch, low substituted hydroxypropyl cellulose, hydroxypropyl cellulose, magnesium stearate

  In the film coat:
  Hypromellose, propylene glycol, titanium dioxide (E171), carnauba wax and iron oxides (see below).
  Uptravi 200 microgram film-coated tablets contain iron oxide yellow (E172).
  Uptravi 400 microgram film-coated tablets contain iron oxide red (E172).
  Uptravi 600 microgram film-coated tablets contain iron oxide red and iron oxide black (E172).
  Uptravi 800 microgram film-coated tablets contain iron oxide yellow and iron oxide black (E172).
  Uptravi 1,000 microgram film-coated tablets contain iron oxide red and iron oxide yellow (E172).
  Uptravi 1,200 microgram film-coated tablets contain iron oxide black and iron oxide red

(E172).
Uptravi 1,400 microgram film-coated tablets contain iron oxide yellow (E172).
Uptravi 1,600 microgram film-coated tablets contain iron oxide black, iron oxide red and iron oxide yellow (E172).

What Uptravi looks like and contents of the pack

Uptravi 200 microgram film-coated tablets: Round, light-yellow, film-coated tablets with "2" marked on one side.

Uptravi 400 microgram film-coated tablets: Round, red, film-coated tablets with "4" marked on one side.

Uptravi 600 microgram film-coated tablets: Round, light-violet, film-coated tablets with "6" marked on one side.

Uptravi 800 microgram film-coated tablets: Round, green, film-coated tablets with "8" marked on one side.

Uptravi 1,000 microgram film-coated tablets: Round, orange, film-coated tablets with "10" marked on one side.

Uptravi 1,200 microgram film-coated tablets: Round, dark-violet, film-coated tablets with "12" marked on one side.

Uptravi 1,400 microgram film-coated tablets: Round, dark-yellow, film-coated tablets with "14" marked on one side.

Uptravi 1,600 microgram film-coated tablets: Round, brown, film-coated tablets with "16" marked on one side.

Uptravi 200 microgram film-coated tablets are supplied in blister packs of 10 or 60 tablets and 60 or 140 tablets (titration packs).

Uptravi 400 microgram, 600 microgram, 800 microgram, 1,000 microgram, 1,200 microgram, 1,400 microgram, and 1,600 microgram film-coated tablets are supplied in blister packs of 60 tablets.

Not all pack sizes may be marketed.

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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.