Uptravi (Selexipag) Titration Phase

The goal of titration is to reach the individually appropriate dose for each patient. This usually happens within 8 weeks.

200 microgram tablet **800 microgram tablet**

- **Titration Pack*:** Start with 200 micrograms twice daily every 12 hours. To improve tolerability, patients should take tablets with food. The first tablet should be taken in the evening.
- **Titrate up:** Increase the dose by 200 micrograms twice daily. Each dosing step lasts about one week, but may take longer. The first dose of each step should be taken in the evening.
- **Patient follow-up:** Increase the dose until side effects that cannot be tolerated or medically managed are experienced.‡
- **Reduce tablet burden†:** If a dose higher than 800 micrograms is needed, patients may be given:
  - Another Uptravi 200 microgram titration pack
  - A pack of Uptravi 800 microgram tablets
- **Step down:** If a patient reaches a dose that cannot be tolerated or medically managed, reduce the dose to the previous level.
- **Maximum dose:** 1,600 micrograms twice daily is the maximum dose a patient should be given (i.e. total daily intake should not exceed 3,200 micrograms).
- **Maintenance Phase:** The highest tolerated dose becomes the individualised maintenance dose and may be replaced with an equivalent single tablet twice daily. This dose should never exceed 1600 micrograms twice daily

STARTING DOSE

Each dosing step lasts about 1 week.

STEP 1
Morning: 1x200 microgram tablet
Evening: 1x200 microgram tablet (total daily dose: 400 microgram)

STEP 2
Morning: 2x200 microgram tablets
Evening: 2x200 microgram tablets (total daily dose: 800 microgram)

STEP 3
Morning: 3x200 microgram tablets
Evening: 3x200 microgram tablets (total daily dose: 1,200 microgram)

STEP 4:
Morning: 4x200 microgram tablets
Evening: 4x200 microgram tablets (total daily dose: 1,600 microgram)

MAXIMUM DOSE

STEP 5
Morning: 1x800 and 1x200 microgram tablet
Evening: 1x800 and 1x200 microgram tablet (total daily dose: 2,000 microgram)

STEP 6
Morning: 1x800 and 2x200 microgram tablets
Evening: 1x800 and 2x200 microgram tablet (total daily dose: 2,400 microgram)

STEP 7
Morning: 1x800 and 3x200 microgram tablets
Evening: 1x800 and 3x200 microgram tablet (total daily dose: 2,800 microgram)

STEP 8
Morning: 1x800 and 4x200 microgram tablets
Evening: 1x800 and 4x200 microgram tablets (total daily dose: 3,200 microgram)

(Tablets are not actual size)

*The titration pack contains 140 Uptravi 200 microgram film-coated tablets. This is enough tablets to titrate up to 800 micrograms.

†The 2 packs have enough tablets to titrate up to 1600 micrograms.

‡The most common side effects your patients may experience while taking Uptravi are: headache, diarrhoea, nausea and vomiting, jaw pain, myalgia, pain in the extremity, arthralgia, flushing and nasopharyngitis (of non-infectious origin). For a full list of side effects see Summary of Product Characteristics for further information. The dosing of Uptravi should be reduced to once daily in patients with moderate hepatic impairment or if co-administered with moderate CYP2C8 inhibitors e.g. clopidogrel, deferasirox and teriflunomide. Dosing frequency of Uptravi should revert to twice daily when co-administration of CYP2C8 inhibitor is stopped.

For dosing, dose adjustments and other information, please consult full prescribing information.

Getting Patients Started

Treatment with Uptravi should only be initiated and monitored by a physician experienced in the treatment of Pulmonary Arterial Hypertension (PAH)

Patient titration pack includes:

- Uptravi 200 microgram film-coated tablets for titration
- A patient titration guide that includes an explanation of the titration process and a diary to record the number of tablets taken daily
  — Upon initiation, be sure to review the titration guide with patients to ensure they fully understand the process and are prepared if they experience side effects

Note: To reduce tablet burden, if a dose higher than 800 micrograms is needed, patients may be given a second Uptravi 200 microgram titration pack and a pack of Uptravi 800 microgram tablet

Patient Communication

- Contact your patients weekly during the titration period to discuss their progress and to ensure that any pharmacological effects are treated effectively
- Side effects associated with the pharmacological action of Uptravi such as headache, diarrhoea, jaw pain, nausea, myalgia, vomiting, pain in extremity, flushing, arthralgia and nasopharyngitis (of non-infectious origin), have been observed frequently, in particular during the individualised dose titration
- Expected pharmacological side effects are usually transient or manageable with symptomatic treatment
- In clinical practice, gastrointestinal (GI) events have been observed to respond to antidiarrhoeal, antiemetic, and antinauseant medications and/or drugs for functional GI disorders. Pain-associated events have been frequently treated with analgesics (such as paracetamol)

Maintenance

- Once a maintenance dose is achieved, an equivalent single-tablet strength for the individualised maintenance dose can be prescribed (200–1600 microgram tablets available)
- This allows the patient to take one tablet in the morning and one in the evening
- Every patient is different and not everyone will end up on the same maintenance dose. No dose should exceed 1600 micrograms twice daily

The single maintenance dose tablets will differ in colour and have numbers stamped into the surface showing the dose (in hundreds of micrograms)

UPTRAVI® film-coated tablets (selexipag)
Tablets are not actual size
Marketing authorisation holder: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium
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