What is selexipag (Uptravi®)?
Selexipag is an oral medication called a prostacyclin IP receptor agonist indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group 1 PH) in WHO Functional Class II and III patients, to delay disease progression and reduce the risk of hospitalization for PAH.

How does selexipag (Uptravi®) work?
Selexipag is an oral prostacyclin IP receptor agonist that is structurally unique from prostacyclin. It is converted to the active form of the drug in the liver, which is 37 times more potent than the parent molecule, and binds directly to a receptor called the IP receptor. Selexipag and its metabolite bind to the IP receptor but not to other types of prostacyclin receptors.

In the GRIPHON study, which enrolled 1,156 patients with PAH (idiopathic PAH, heritable PAH, PAH associated with corrected-congenital shunts, PAH associated with connective tissue disease, PAH associated with drug or toxin exposure, and HIV-associated PAH), treatment with selexipag resulted in a 40% risk reduction in the composite endpoint of death or a complication related to PAH, mainly due to patients experiencing a hospitalization or a pre-defined sign of disease progression. This significant beneficial effect was seen in patients who were not yet on treatment for PAH when enrolled in the trial as well as in patients who were already on another medication, i.e., background therapy (phosphodiesterase inhibitor and/or endothelin receptor antagonist).¹

How is selexipag (Uptravi®) given?
Selexipag is an oral tablet given by mouth.

Dosing of selexipag (Uptravi®)
The starting dose of selexipag is 200 mcg twice daily. The dose is then increased by 200mcg twice daily every week to the highest dose a patient can tolerate up to a maximum dose of 1,600mcg twice daily. The long-term (i.e. maintenance) dose is determined by how well the patient tolerates side effects – i.e. during the dose titration phase the dose is increased until the patient has intolerable side effects. Tolerability may be improved if the drug is taken with food.

How is selexipag (Uptravi®) supplied?
Selexipag is supplied in bottles of 60 tablets in the following doses: 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1,000 mcg, 1,200 mcg, 1,400 mcg, or 1,600 mcg.

Selexipag is also supplied in a dose titration pack that includes a 140-count bottle of 200 mcg tablets and a 60-count bottle of 800 mcg tablets.³

Once a patient reaches their maximally tolerated (maintenance) dose, the medication can be prescribed so that they only take one selexipag tablet in the morning and one selexipag tablet in the evening.
How do patients obtain selexipag (Uptravi®)?
Patients obtain selexipag through a prescription from their pulmonary hypertension specialist.

Will insurance pay for selexipag (Uptravi®)?
It is expected that most health insurance plans will pay part of the cost of this medication. However, some plans still leave patients with a high out-of-pocket responsibility.

Depending on your insurance type, you may be eligible for assistance from the company that manufactures your therapy or from a non-profit charitable assistance organization. For more information visit www.PHAssociation.org/Help or call 301-565-3004.

How is selexipag (Uptravi®) initiated?
After the prescribing provider completes the patient enrollment form to obtain prior authorization through insurance and it is approved, selexipag is initiated at 200mcg by mouth twice daily as an outpatient.

What are the main side effects of selexipag (Uptravi®)?
The side effects of selexipag reported from GRIPHON are similar to the side effects from prostacyclins and include:

- Headache
- Diarrhea
- Jaw pain
- Nausea
- Myalgia (muscle pain)
- Vomiting
- Pain in Extremity
- Flushing
- Arthralgia (joint pain)
- Anemia
- Decreased appetite
- Rash

These side effects are seen more when patients are actively increasing the dose, while attempting to determine the long-term stable maintenance dose.1 Hyperthyroidism (overactive thyroid) has also been seen in patients on selexipag.3
What are considerations for the use of selexipag (Uptravi®) in special populations?

Pregnancy – There are no adequate and well-controlled studies in pregnant women. However, in most circumstances we recommend you do not become pregnant while being treated for PAH. In animal studies, slight reductions in maternal and fetal weights were seen in rats when pregnant rats were given selexipag at dose exposure approximately 47-times the maximum human dose during organogenesis, but there was no evidence of other abnormalities. There were no developmental abnormalities seen when pregnant rabbits were given selexipag at dose exposure 50-times the maximum human dose.³

Lactation – Although it is not known whether selexipag is found in human milk, it has been detected in milk from lactating rats. Due to the fact that many drugs are present in milk and due to possible adverse effects to the fetus on exposure to selexipag, it is advised that a nursing mother either discontinue nursing or discontinue selexipag.³ In most circumstances, however, we recommend that you do not become pregnant while being treated for PAH.

Pediatric Use – Safety and effectiveness in pediatric patients is not known.

Geriatric Use – Of the 1,368 patients in clinical studies, 248 subjects were older than 65 and 19 subjects were 75 or older. No significant differences have been seen or reported in older patients compared to younger patients, but a greater sensitivity to the medication cannot be ruled out.³

Patients with Liver Impairment – No dose adjustment is required in patients with mild liver impairment (Child-Pugh Class A). It is recommended that selexipag be given only once daily in patients with moderate liver impairment (Child-Pugh Class B) and that it not be used in patients with severe liver impairment (Child-Pugh Class C).³

Patients with Renal Impairment – No dose adjustment is required in patients with a glomerular filtration rate (GFR) > 15 ml/min/1.73 m². There is no clinical experience in patients with a GFR < 15 ml/min/1.73 m² or who are undergoing dialysis.³

Could a patient be allergic to selexipag (Uptravi®)?

It is possible, but unlikely.

What are important drug interactions with selexipag (Uptravi®)?

Patients should avoid concomitant use of strong inhibitors of CYP2C8 such as gemfibrozil, which may increase patient exposure to selexipag and its active metabolite. No dose adjustments are recommended for other PAH medications, warfarin, or lopinivir/ritonavir.³
Are there other ways of administering selexipag (Uptravi®)?
No, it is only available as a tablet taken by mouth. It also cannot be crushed and given via a feeding tube or through an IV. This is important to know because if a patient must be NPO (have nothing by mouth) for any reason, the prescriber must have an alternative treatment plan in place to treat them through that period of time.

References:
3. For full prescribing details, see prescribing information available at uptravi.com.