Uptravi

(selexipag)

New Product Slideshow

MPR

Introduction

- **Brand name:** Uptravi
- **Generic name:** Selexipag
- **Pharmacological class:** Prostacyclin receptor antagonist
- **Strength and Formulation:** 200mcg, 400mcg, 600mcg, 800mcg, 1000mcg, 1200mcg, 1400mcg, 1600mcg; tablets
- **Manufacturer:** Actelion
- **How supplied:** Bottle—60, 140 (see labeling); Titration pack—1 (140x200mcg tabs) + (60x800mcg tabs)
- **Legal Classification:** Rx

Indications

- **Pulmonary arterial hypertension** (PAH) (WHO Group 1) in patients with WHO functional Class II–III symptoms, to delay disease progression and reduce the risk of hospitalization for PAH

Dosage & Administration

- Swallow whole; may take with food to improve tolerability
- Initially 200mcg twice daily; increase by 200mcg increments twice daily at weekly intervals to highest tolerated dose up to 1600mcg twice daily; reduce to previous dose if not tolerated
- **Moderate hepatic impairment** (Child-Pugh class B): initially 200mcg once daily; increase in 200mcg increments once daily at weekly intervals as tolerated

Considerations for Special Populations

- **Pregnancy:** No adequate studies in pregnant women
- **Nursing mothers:** Not recommended
- **Pediatric:** Not established
- **Geriatric:** No overall differences observed
- **Renal impairment:** Dialysis or GFR <15mL/min/1.73m^2: not studied
- **Hepatic impairment:** Severe impairment: avoid

Warnings/Precautions

- **Discontinue** if pulmonary veno-occlusive disease confirmed

Interactions

- May be potentiated by concomitant strong CYP2C8 inhibitors (eg, gemfibrozil); **avoid**

Adverse Reactions

- Headache
- Diarrhea
- Jaw pain
- Nausea
- Myalgia
- Vomiting
- Pain in extremity
- Flushing
- Arthralgia
- Anemia
- Decreased appetite
- Rash

Mechanism of Action

- **Selexipag** is an oral prostacyclin receptor (IP receptor) agonist that is structurally distinct from prostacyclin
- Hydrolysis of selexipag in the liver yields an active metabolite; both selexipag and its active metabolite selectively target the IP receptor vs. other prostanoid receptors (EP1-4, DP, FP, TP)

Pharmacokinetics

- **Distribution:** ~99% bound to plasma proteins
- **Metabolism:** CYP3A4, CYP2C8, UGT1A3, UGT2B7
- **Elimination:** Fecal

Clinical Trials

- The effect of selexipag was evaluated in the **GRIPHON** study, a multicenter, double-blind, placebo-controlled, parallel-group, event-driven trial of 1,156 patients with symptomatic (WHO Functional Class I [0.8%], II [46%], III [53%], and IV [1%]) pulmonary arterial hypertension (PAH)

Clinical Trials

- The study's primary endpoint was the time to first occurrence up to end-of-treatment of:
  - Death
  - Hospitalization for PAH
  - PAH worsening resulting in need for lung transplantation, or balloon atrial septostomy
  - Initiation of parenteral prostanoid therapy or chronic oxygen therapy, or
  - Other disease progression based on a 15% decrease from baseline in 6-Minute Walk Distance (6MWD) plus worsening of Functional Class or need for additional PAH-specific therapy

Clinical Trials

- Study results showed that patients treated with selexipag had a **40%** reduction (99% CI: 22 to 54%; *P*<0.0001) of the occurrence of primary endpoint events compared to placebo
- The beneficial effect of selexipag was primarily attributed to a reduction in hospitalizations for PAH (13.6% vs. 18.7% in placebo) and a reduction of other disease progression events (6.6% vs. 17.2% in placebo)
- The observed benefit of selexipag was similar regardless of the dose achieved after titration

Clinical Trials

- More deaths as a first event were observed in the selexipag group (4.9%) vs. placebo group (3.1%); however, such deaths were too few to determine whether they were drug-related
- The treatment effect of selexipag on time to first primary event was consistent irrespective of background PAH therapy (eg, with ERA, PDE-5 inhibitors, or both, or without background therapy)

Clinical Trials

- Exercise capacity was also evaluated as a secondary outcome for the study
- Selexipag resulted in a median absolute change from baseline to week 26 in 6MWD (measured at ~12 hours post-dose) of +4 meters vs. −9 meters for placebo
- This resulted in a placebo-corrected median treatment effect of 12 meters (99% CI: 1, 24; *P*=0.005)
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the complete product monograph available at:

  http://www.empr.com/uptravi/drugproduct/406/