1 April 2016
EMA/CHMP/826224/2015 Rev. 1
Committee for Medicinal Products for Human Use (CHMP)

**Summary of opinion[1] (initial authorisation)**

# Uptravi

selexipag

On 1 April 2016 the Committee for Medicinal Products for Human Use (CHMP) adopted a revised positive opinion, recommending the granting of a marketing authorisation for the medicinal product Uptravi, intended for the treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO functional class (FC) II-III.

Uptravi was designated as an orphan medicinal product on 26 August 2005. The applicant for this medicinal product is Actelion Registration Ltd. At the time of the review of the orphan designation by the Committee on Orphan Medicinal Products (COMP), this product was withdrawn from the Community Register of designated orphan medicinal products on 17 February 2016 at the request of the sponsor.

Uptravi will be available as 200 µg, 400 µg, 600 µg, 800 µg, 1,000 µg, 1,200 µg, 1,400 µg and 1,600 µg film-coated tablets. The active substance of Uptravi is selexipag, an orally available, selective prostacyclin (IP) receptor agonist that is distinct from prostacyclin and its analogues. The ATC code is B01AC27, antithrombotic agents, platelet aggregation inhibitors excluding heparin. By activating the IP receptor, selexipag leads to vasodilatation and inhibition of platelet aggregation. However, at clinically relevant concentrations, there was no effect on platelet aggregation test parameters.

The benefits with Uptravi in patients with PAH are its ability to dilate the pulmonary arteries as well as its anti-proliferative and anti-fibrotic effects, which decrease pulmonary arterial pressure and delay disease progression. Each patient should be up-titrated to the highest individually tolerated dose, from a starting dose of 200 micrograms given twice daily up to a maximum of 1,600 micrograms given twice daily.

The most common side effects are headache, diarrhoea, nausea and vomiting, jaw pain, myalgia, pain in extremity, arthralgia and flushing. These reactions are more frequent during the up-titration phase. The majority of these reactions are of mild to moderate intensity.

The full indication is: "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.

[1] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued 67 days from adoption of the opinion

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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 (see section 5.1)."

Uptravi should only be initiated and monitored by a physician experienced in the treatment of PAH.

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and made available in all official European Union languages after the marketing authorisation has been granted by the European Commission.