EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 October 2013
EMA/CHMP/590387/2013
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Opsumit

macitentan

On 24 October2013, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Opsumit 10mg film coated tablet intended for the treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.

Opsumit was designated as an orphan medicinal product on 29 September 2011. The applicant for this medicinal product is Actelion Registration Ltd. They may request a re-examination of any CHMP opinion, provided they notify the European Medicines Agency in writing of their intention within 15 days of receipt of the opinion.

The active substance of Opsumit is macitentan an orally active, dual Endothelin (ET) A and EndothelinB receptor antagonist, ATC code: C02KX04.

Macitentan displays high affinity and sustained occupancy of the ET receptors in human pulmonary arterial smooth muscle cells. This prevents endothelin-mediated activation of second messenger systems that result in vasoconstriction and smooth muscle cell proliferation.

The benefits with Opsumit are its ability to provide a clinically relevant effect of macitentan 10 mg to reduce the risk of occurrence of the primary endpoint in the study population. The primary endpoint of the Seraphin pivotal study was the time to first occurrence of a clinical worsening event, up to the end of double-blind treatment, defined as death, or atrial septostomy, or lung transplantation, or initiation of intravenous (i.v.) or subcutaneous (s.c.) prostanoids, or other worsening of PAH.

The treatment effect with macitentan on the primary endpoint was established early and was sustained during treatment (median duration of more than 2 years). For the 10 mg dose it corresponded to an overall relative risk reduction of 45% (absolute risk reduction of 16%) and a number-needed-to-treat (NNT) of 6 patients (95% CLs 4.48, 10.80) to avoid one event at 2 years.

The most common side effects are nasopharyngitis (14.0%), headache (13.6%) and anaemia (13.2%). The majority of adverse events are mild to moderate in intensity.

[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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A pharmacovigilance plan for Opsumit will be implemented as part of the marketing authorisation. The approved indication is:

“Opsumit, as monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.

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)".

It is proposed that the treatment 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.

The CHMP, on the basis of quality, safety and efficacy data submitted, considers there to be a favourable benefit-to-risk balance for Opsumit and therefore recommends the granting of the marketing authorisation.