European Medicines Agency
Pre-Authorisation Evaluation of Medicines for Human Use

London, 21 February 2008
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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
SUMMARY OF POSITIVE OPINION*
for
VOLIBRIS

International Nonproprietary Name (INN): ***ambrisentan***

On 21 February 2008 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion,** recommending to grant a marketing authorisation for the medicinal product Volibris, 5 mg and 10 mg, Film coated tablets intended for treatment of pulmonary arterial hypertension. Volibris was designated as an orphan medicinal product on 11 April 2005. The applicant for this medicinal product is Glaxo Group Limited.

The active substance of Volibris is ambrisentan, an anti-hypertensives medicinal product (C02KX02). Ambrisentan is an endothelin receptor antagonist (ERA) that is selective for the endothelin type A (ET_A) receptor. ET_A receptor antagonists inhibit phospholipase C-mediated vasoconstriction and protein kinase C-mediated cell proliferation, while preserving nitric oxide (NO) and prostacyclin production, cyclic GMP- and cyclic AMP-mediated vasodilation, and endothelin-1 (ET-1) clearance that is associated with the endothelin type B (ET_B) receptor.

The benefits with Volibris are efficacy in improving exercise capacity in patients with idiopathic pulmonary arterial hypertension (PAH) classified as WHO functional class II and III, and pulmonary arterial hypertension associated with connective tissue disease. The most common side effects are headache, flushing, nasal symptoms (especially congestion) and peripheral oedema.

A pharmacovigilance plan for Volibris, as for all medicinal products, will be implemented as part of the marketing authorisation.

The approved indication is: "Volibris is indicated for the treatment of patients with pulmonary arterial hypertension (PAH) classified as WHO functional class II and III, to improve exercise capacity (see section 5.1). Efficacy has been shown in idiopathic PAH (IPAH) and in PAH associated with connective tissue disease". It is proposed that Volibris is prescribed by physicians experienced in the treatment of pulmonary arterial hypertension.

Detailed recommendations for the use of this product will be described in the Summary of Product Characteristics (SPC) which will be published in the European Public Assessment Report (EPAR) and will be 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 that there is a favourable benefit to risk balance for Volibris and therefore recommends the granting of the marketing authorisation.

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* Summaries of positive opinion are published without prejudice to the Commission Decision, which will normally be issued within 67 days from adoption of the Opinion.

** Applicants may request a re-examination of any CHMP opinion, provided they notify the EMEA in writing of their intention to request a re-examination within 15 days of receipt of the opinion.

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