24 September 2015
EMA/CHMP/617813/2015
Committee for Medicinal Products for Human Use (CHMP)

**Summary of opinion1 (initial authorisation)**

# Orkambi

## lumacaftor / ivacaftor

On 24 September 2015, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Orkambi, intended for the treatment of cystic fibrosis (CF). Orkambi was designated as an orphan medicinal product on 22 August 2014. The applicant for this medicinal product is Vertex Pharmaceuticals (Europe) Ltd.

Orkambi is a fixed-dose combination of two active substances, lumacaftor and ivacaftor, and will be available as 200 mg/125 mg film-coated tablets (ATC code: R07AX30). Orkambi is to be used in patients with the specific F508del mutation affecting the CF transmembrane conductance regulator (CFTR) gene. This gene encodes for the CFTR protein which is a chloride channel normally present at the surface of epithelial cells in multiple organs. Lumacaftor improves the cellular processing and trafficking of the F508del-CFTR protein to the cell membrane, while ivacaftor facilitates the function of the CFTR protein by increasing the CFTR channel gating. The combined effect of lumacaftor and ivacaftor results in increased quantity and function of F508del-CFTR protein at the cell surface, resulting in increased chloride ion transport.

The benefits of Orkambi are its ability to improve pulmonary function [measured as the absolute change from baseline in percent predicted forced expiratory volume in 1 second (ppFEV1)], increase the body weight and decrease the rate of pulmonary exacerbations in CF patients homozygous with F508del-CFTR. Mean improvement in ppFEV1, although of limited magnitude, was rapid in onset (15 days after starting treatment), sustained throughout the 48 week treatment period and observed regardless of age, disease severity, sex and geographic region. The most common side effects in patients aged 12 years and older who received lumacaftor/ivacaftor were dyspnoea, diarrhoea, and nausea.

The full indication is: "Orkambi is indicated for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who are homozygous for the F508del mutation in the CFTR gene (see sections 4.4 and 5.1)."

It is proposed that Orkambi be prescribed by physicians experienced in the treatment of CF. If the patient's genotype is unknown, an accurate and validated genotyping method should be performed to

[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

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
**Telephone** +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
**Send a question via our website** www.ema.europa.eu/contact

confirm the presence of the F508del mutation on both alleles of the CFTR gene.

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.