25 June 2020
EMA/CHMP/308597/2020
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Kaftrio

elexacaftor / tezacaftor / ivacaftor

On 25 June 2020, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Kaftrio[2], intended for the treatment of cystic fibrosis in patients aged 12 years and older who are homozygous for the *F508del* mutation or heterozygous for the F508del in the *CFTR* gene with a minimal function mutation (MF) (corresponding to either no production of a CFTR protein or a CFTR protein that is not responsive to ivacaftor and tezacaftor/ivacaftor *in vitro)*.

Kaftrio was initially reviewed under EMA's accelerated assessment programme. However, during assessment, this could no longer be achieved, since the applicant requested a 3-month clock stop ultimately reduced to 2 months. Therefore, the conditions for accelerated assessment could not be met.

The applicant for this medicinal product is Vertex Pharmaceuticals (Ireland) Limited.

Kaftrio will be available as film-coated tablets containing 100 mg elexacaftor, 50 mg tezacaftor and 75 mg ivacaftor (ATC code: R07AX). Elexacaftor and tezacaftor are CFTR correctors and facilitate the cellular processing and trafficking of F508del-CFTR, leading to an increase in the amount of CFTR protein, while ivacaftor increases channel gating of the CFTR protein at the cell surface. The combined effect of elexacaftor, tezacaftor and ivacaftor results in increased CFTR activity as measured by CFTR chloride transport.

The benefits with Kaftrio are its ability to provide significant improvements in lung function as measured by ppFEV1 (percent predicted FEV1) (14.3 percentage point reduction in heterozygous MF and 10 percentage point reduction in homozygous patients) and to reduce sweat chloride (a reduction of 41.8 mmol/L in MF and 45.1 mmol/L in homozygous patients).

The most common adverse reactions were headache (17.3%), diarrhoea (12.9%) and upper respiratory tract infection (11.9%).

The full indication is:

[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
[2] This product was designated as orphan medicine during its development. EMA will now review the information available to date to determine if the orphan designation can be maintained

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Kaftrio is indicated in a combination regimen with ivacaftor 150 mg tablets for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who are homozygous for the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene or heterozygous for *F508del* in the *CFTR* gene with a minimal function (MF) mutation.

It is proposed that Kaftrio is prescribed by physicians experienced in the treatment of cystic fibrosis.

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.