EMA/352917/2020
EMEA/H/C/005269

Kaftrio (ivacaftor / tezacaftor / elexacaftor)

An overview of Kaftrio and why it is authorised in the EU

What is Kaftrio and what is it used for?

Kaftrio is a medicine used to treat patients aged 12 years and above who have cystic fibrosis, an inherited disease that has severe effects on the lungs, the digestive system and other organs.

Cystic fibrosis can be caused by various mutations (changes) in the gene for a protein called 'cystic fibrosis transmembrane conductance regulator' (CFTR). People have 2 copies of this gene, one inherited from each parent and the disease only occurs when there is a mutation in both copies.

Kaftrio is used in patients whose cystic fibrosis is due to the *F508del* mutation inherited from one or both parents. If they have inherited this mutation from only one parent, they should also have another mutation called a 'minimal function mutation' from the other parent.

Cystic fibrosis is rare, and Kaftrio was designated an 'orphan medicine' (a medicine used in rare diseases) on 14 December 2018. Further information on the orphan designation can be found here: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3182117

Kaftrio contains the active substances ivacaftor, tezacaftor and elexacaftor.

How is Kaftrio used?

The medicine can only be obtained with a prescription. Kaftrio should only be prescribed by a healthcare professional with experience in the treatment of cystic fibrosis.

Kaftrio is available as tablets. Each tablet contains 75 mg ivacaftor, 50 mg tezacaftor and 100 mg elexacaftor. Kaftrio should be taken together with another medicine containing ivacaftor alone. The recommended daily dose is two tablets of Kaftrio in the morning with fat-containing food and one ivacaftor tablet (150 mg) in the evening, about 12 hours later.

The doses of Kaftrio and ivacaftor may need to be reduced if the patient is also taking a type of medicine called a 'moderate or strong CYP3A inhibitor', such as certain antibiotics or medicines for fungal infections. The doctor may need to adjust the dose in patients with reduced liver function.

For more information about using Kaftrio, see the package leaflet or contact your doctor or pharmacist.

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

How does Kaftrio work?

Cystic fibrosis is caused by mutations in the CFTR gene. This gene leads to the production of the CFTR protein, which works on the surface of cells to regulate the production of mucus in the lungs and digestive juices in the gut. The mutations reduce the number of CFTR proteins on the cell surface or affect the way the protein works, resulting in secretions of the cells that make mucus and digestive fluids being too thick and leading to blockages, inflammation, increased risk of lung infections, and poor digestion and growth.

Two of the active substances in Kaftrio, elexacaftor and tezacaftor, increase the number of CFTR proteins on the cell surface and the other, ivacaftor, improves the activity of the defective CFTR protein. These actions combine to make lung mucus and digestive juices less thick, thereby helping to relieve symptoms of the disease.

What benefits of Kaftrio have been shown in studies?

Kaftrio taken together with ivacaftor was effective at improving lung function in two main studies in patients with cystic fibrosis aged 12 years and above. The main measure of effectiveness was ppFEV1, which is the maximum amount of air a person can breathe out in one second compared with values from an average person with similar characteristics (such as age, height and sex). In these studies, patients started off with values of 60 to 62% of the values from an average healthy person.

The first study involved 403 patients who have a *F508del* and an MF mutation. After 24 weeks of treatment, patients who took Kaftrio and ivacaftor had an average increase in ppFEV1 of 13.9 percentage points compared with a reduction of 0.4 percentage points in patients who took placebo (a dummy treatment).

In the second study involving 107 patients with a *F508del* mutation from both parents, patients who took Kaftrio with ivacaftor had an average increase in ppFEV1 of 10.4 percentage points compared with an increase of 0.4 percentage points in patients who took a combination of ivacaftor and tezacaftor alone.

What are the risks associated with Kaftrio?

The most common side effects with Kaftrio (which may affect more than 1 in 10 people) are headache, diarrhoea and upper respiratory tract infection (nose and throat infection). Rashes may occur and sometimes be serious.

For the full list of side effects and restrictions of Kaftrio, see the package leaflet.

Why is Kaftrio authorised in the EU?

Kaftrio is an effective treatment for patients with cystic fibrosis who have two *F508del* mutations or one *F508del* and one MF mutation. Both are groups with a high unmet medical need. Patients with one *F508del* mutation plus other mutations were not covered in the studies, and although the company submitted some data on use in such patients, further data was considered necessary to support authorisation in these groups. In terms of safety, Kaftrio was well tolerated. Therefore, the European Medicines Agency decided that Kaftrio's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Kaftrio?

The company that markets Kaftrio will carry out a study on the long-term safety of Kaftrio including in pregnant women.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Kaftrio have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Kaftrio are continuously monitored. Side effects reported with Kaftrio are carefully evaluated and any necessary action taken to protect patients.

Other information about Kaftrio

Kaftrio received a marketing authorisation valid throughout the EU on 21 August 2020.

Further information on Kaftrio can be found on the Agency's website: https://www.ema.europa.eu/en/medicines/human/EPAR/kaftrio

This overview was last updated in 08-2020.