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Symkevi (*tezacaftor / ivacaftor*)

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

What is Symkevi and what is it used for?

Symkevi is a medicine used to treat cystic fibrosis in patients aged 12 years and above. Cystic fibrosis is an inherited disease that has severe effects on the lungs, the digestive system and other organs. Cystic fibrosis affects the cells that produce mucus and digestive juices. As a result, these secretions become thick and cause blockage. Build-up of thick and sticky secretions in the lungs causes inflammation and long-term infection. In the gut, blockage of the tubes from the pancreas slows down the digestion of food and causes poor growth.

Symkevi is used in patients who have a mutation (change) called *F508del* in the gene for a protein called 'cystic fibrosis transmembrane conductance regulator' (CFTR).

Symkevi is used in patients who have inherited the *F508del* mutation from both parents and therefore have the mutation in both copies of the *CFTR* gene. It is also used in patients who have inherited the *F508del* mutation from one parent and also have one of the following mutations in *CFTR*: *P67L*, *R117C*, *L206W*, *R352Q*, *A455E*, *D579G*, *711+3A→G*, *S945L*, *S977F*, *R1070W*, *D1152H*, *2789+5G→A*, *3272 26A→G*, or *3849+10kbC→T*.

Symkevi contains the active substances tezacaftor and ivacaftor.

Cystic fibrosis is rare, and Symkevi was designated an 'orphan medicine' (a medicine used in rare diseases) on 27 February 2017. Further information on the orphan designation can be found here: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

How is Symkevi used?

Symkevi should only be prescribed by a doctor with experience in the treatment of cystic fibrosis, and only in patients confirmed to have the mutations mentioned above.

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

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The doses of Symkevi and ivacaftor may need to be adjusted 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 doses may also need to be adjusted in patients with reduced liver function.

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

How does Symkevi work?

Cystic fibrosis is caused by mutations in the *CFTR* gene. This gene makes the CFTR protein, which works on the surface of cells to regulate the production of mucus and digestive juices. The mutations reduce the number of CFTR proteins on the cell surface or affect the way the protein works.

One of the active substances in Symkevi, tezacaftor, increases the number of CFTR proteins on the cell surface and the other, ivacaftor, increases the activity of the defective CFTR protein. These actions make mucus and digestive juices less thick, thereby helping to relieve symptoms of the disease.

What benefits of Symkevi have been shown in studies?

Symkevi taken together with ivacaftor was shown to be effective at improving lung function in two main studies of patients with cystic fibrosis aged 12 years and above. The main measure of effectiveness was based on improvement in patients' FEV_1. FEV_1 is the maximum amount of air a person can breathe out in one second and is a measure of how well the lungs work.

The first study involved 510 patients with cystic fibrosis who have inherited the *F508del* mutation from both parents. Symkevi, taken with ivacaftor, was compared with placebo (a dummy treatment). After 24 weeks of treatment, patients who took the medicines had an average increase in FEV_1 of 3.4 percentage points compared with a reduction of 0.6 percentage points in patients who took placebo.

The second study involved 248 patients with cystic fibrosis who have inherited the *F508del* mutation from one parent and who also have another *CFTR* mutation. Symkevi, taken with ivacaftor, was compared with ivacaftor taken alone and with placebo. Lung function was measured after 4 weeks and 8 weeks of treatment. Patients who took Symkevi and ivacaftor had an average increase in FEV_1 of 6.5 percentage points compared with an increase of 4.4 percentage points in patients who took ivacaftor alone and a reduction of 0.3 percentage points in patients who took placebo.

What are the risks associated with Symkevi?

The most common side effects with Symkevi (which may affect more than 1 in 10 people) are headache and nasopharyngitis (inflammation of the nose and throat).

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

Why is Symkevi authorised in the EU?

Symkevi is an effective treatment for patients with cystic fibrosis who have inherited the *F508del* mutation from both parents or patients who have the *F508del* mutation from one parent and certain other mutations. In the former group, Symkevi could especially be a treatment option for those who cannot take a combination of ivacaftor and lumacaftor (another cystic fibrosis medicine), due to side effects or interactions with other medicines they are taking. In the latter group, there is a lack of authorised therapies. Therefore, the European Medicines Agency decided that Symkevi'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 Symkevi?

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

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

Other information about Symkevi

Symkevi received a marketing authorisation valid throughout the EU on 31 October 2018.

Further information on Symkevi can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

This overview was last updated in 10-2018.