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Trikafta® (active substances: elexacaftor, ivacaftor, tezacaftor)

First authorisation in Switzerland: 10 December 2020

Medicine (film-coated tablets) for the treatment of cystic fibrosis

About the medicinal product

The medicinal product Trikafta, containing the active substances elexacaftor, ivacaftor and tezacaftor, is used for the treatment of patients aged 12 years and older with cystic fibrosis and certain genetic mutations in the "CFTR gene" (CFTR = Cystic Fibrosis Transmembrane Conductance Regulator).

Cystic fibrosis (CF) is a genetic disease caused by a deficiency and/or dysfunction of CFTR. The CFTR gene codes for a protein used for transporting water and salts. A dysfunction of the CFTR protein can lead, for example, to the formation of thick mucus in the lungs or pancreas.

Various defects of the CFTR gene can lead to cystic fibrosis. The most common defect is the lack of coding for phenylalanine (F508del). Around 45% of patients with cystic fibrosis have this type of defect in both sets of chromosomes, which leads to an extensive CFTR malfunction in sufferers and thus to severe cystic fibrosis. In addition, there are a number of other mutations that impair CFTR function in various ways and to varying extents.

Since this is a rare disease, the medicine has been authorised as an orphan drug. The term "orphan drug" refers to important medicines for rare diseases that meet specific requirements. Medicinal products of this kind benefit from simplified authorisation conditions in Switzerland.

Mode of action

In addition to a number of symptomatic treatments, various active substances which, depending on the mutation involved, can improve the function of defective CFTR protein (known as CFTR potentiators) have been available for a few years.

Some of these are authorised only for specific defects in the CFTR gene. One such CFTR potentiator is the active substance ivacaftor. For ivacaftor to be able to work, CFTR proteins must be present on the cell surface, and this active substance only works on so-called "gating defects"[1]. The active substance tezacaftor is used only in combination with

ivacaftor. Tezacaftor can improve the formation and the transport of CFTR proteins to the cell surface. This combination also works in F508del defects.

In addition to the active substances ivacaftor and tezacaftor, Trikafta contains the third active substance elexacaftor. Elexacaftor can also improve the formation and the transport of CFTR proteins to the cell surface, but works in a different way than tezacaftor. It can be used only in the newly authorised combination with all three active substances to produce a functional improvement in F508del defects.

Use

Trikafta is available on prescription only and contains two different film-coated tablets (morning dose and evening dose). The morning dose contains 100 mg of elexacaftor, 50 mg of tezacaftor and 75 mg of ivacaftor. The active substances are combined in a single tablet. The evening dose only contains 150 mg of ivacaftor.

The usual dosage is two film-coated tablets as the morning dose and one film-coated tablet as the evening dose. The morning and evening doses should be taken approximately 12 hours apart.

The tablets may not be broken, chewed or dissolved and should be taken with a fat-containing meal.

Efficacy

The efficacy of Trikafta was investigated mainly in two studies with patients suffering from cystic fibrosis.

One study lasted for 24 weeks and included 403 patients aged 12 years and older. The patients had an F508del mutation on one chromosome and a different CFTR defect on the other, resulting in a failure of the CFTR protein. Trikafta was tested against a dummy drug (placebo). The treatment with Trikafta produced a statistically significant improvement in lung function compared to placebo. The average improvement was rapid in onset and persisted for the full 24-week treatment period.

A shorter 4-week study that tested Trikafta against tezacaftor/ivacaftor recruited 107 patients aged 12 years and older. These patients had an F508del mutation on both chromosomes. The treatment with Trikafta produced a statistically significant improvement in lung function compared to the treatment with tezacaftor/ivacaftor.

Precautions, undesirable effects & risks

Trikafta may not be used in those who are hypersensitive to one of the active substances or any of the excipients.

The most common side effects of Trikafta are skin rash, headache, dizziness, upper respiratory tract infections (common cold), sore throat, nasal congestion, gastric or abdominal pain, diarrhoea, increased liver enzymes (sign of stress on the liver) or a change in the type of bacteria in mucus.

All precautions, risks and other possible side effects are listed in the Information for patients (package leaflet) and the Information for healthcare professionals.

Why the medicine has been authorised

The submitted studies did not investigate all gene defects that can lead to cystic fibrosis.

In particular, the combination of F508del with mild defects on the other chromosome was not investigated.

However, the studies did show that patients aged 12 years and older with cystic fibrosis and certain genetic defects in the CFTR gene can benefit from treatment with Trikafta, showing an improvement in disease symptoms.

Taking all the risks and precautions into account, and based on the available data, the benefits of Trikafta outweigh the risks. Swissmedic has therefore authorised the medicinal product Trikafta, with the active substances elexacaftor, tezacaftor and ivacaftor, in Switzerland, where the benefit for gene defects is expected to be greater than the risk. The patients concerned either possess an F508del defect on both chromosomes or an F508del defect on one chromosome together with a defect on the second chromosome that prevents the formation of CFTR protein (so-called "minimal function mutation").

Further information on the medicinal product

Information for healthcare professionals:
Information for healthcare professionals Trikafta®

Information for patients (package leaflet):
Information for patients Trikafta®

Healthcare professionals (doctors, pharmacists and others) can answer any further questions.

[1]Gating defect: A defect (mutation) in the structure of the CFTR protein that results in the formation of a CFTR protein channel that fails to open correctly.

The date of revision of this text corresponds to that of the SwissPAR. New information concerning the authorised medicinal product in question will not be incorporated into the Public Summary SwissPAR.

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