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

Indication extension in Switzerland: 14 September 2021

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

About the medicinal product

The medicinal product Trikafta contains the active substances elexacaftor, ivacaftor and tezacaftor.

Trikafta has already been authorised by Swissmedic, since 10 December 2020, for the treatment of patients aged 12 years and older with cystic fibrosis (CF) who 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").

With the indication extension, Trikafta can now also be used for the treatment of patients aged 12 years and older with cystic fibrosis (CF) who have at least one F508del mutation 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 and life-threatening disease, the medicine has been authorised as an orphan drug. The term "orphan drug" refers to important medicines for rare diseases.

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 and 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

For the first authorisation, two studies investigating the efficacy of Trikafta were pivotal. These studies investigated CF patients who had a 508del defect on both chromosomes or an F508del defect on one chromosome and an MF mutation ("minimal function mutation") on the second chromosome. It can be assumed that these investigated mutations manifest themselves clinically as serious illnesses.

For the requested indication extension, study 104 was particularly important for evaluating efficacy. This study investigated CF patients who, in addition to the F508 mutation in one chromosome, also possess a second mutation for which treatment with ivacaftor on its own or in combination with tezacaftor is authorised. After a 4-week treatment with ivacaftor or tezacaftor/ivacaftor, a total of 258 patients were then treated for 8 weeks either with Trikafta or tezacaftor/ivacaftor.

The treatment with Trikafta produced a statistically significant improvement in lung function compared to the start of treatment, but also compared to the treatment with tezacaftor/ivacaftor. The average improvement was rapid in onset and persisted for the full 8-week treatment period.

[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.

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 medicinal product has been authorised

The submitted additional study 104 shows that Trikafta is also beneficial in cases of cystic fibrosis with F508del defects on just one chromosome and a second mutation on the other chromosome for which treatment with ivacaftor on its own or in combination with tezacaftor is authorised. However, second mutations that are associated with only a slight functional impairment were not specifically investigated in this study. Overall, it is not clear from the data whether patients who only have very mild cystic fibrosis are able to obtain sufficient benefit from Trikafta.

The diagnostic criteria for cystic fibrosis that are commonly used in Switzerland currently include criteria that require a certain severity of disease. Swissmedic therefore assumes that all patients with heterozygous F508del mutations who meet the diagnostic criteria are seriously ill enough to ensure that the benefit of the treatment with Trikafta in the extended indication outweighs the risks.

Swissmedic has therefore also authorised the medicinal product Trikafta, with the active substances elexacaftor, tezacaftor and ivacaftor, in Switzerland for the treatment of patients aged 12 years and older who have an F508del defect on at least one chromosome.

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.

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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