

Public Summary SwissPAR dated 25.05.2022

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

Indication extension in Switzerland: 5 January 2022

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 who either possess an F508del defect on two chromosomes¹ or an F508del defect on one chromosome together with a defect on the second chromosome that prevents the formation of a functional "CFTR² protein" (so-called "minimal function mutation").

On 14 September 2021, the authorised indication for Trikafta was extended to include the treatment of patients aged 12 years and older with cystic fibrosis who have at least one F508del mutation (defect) in the "CFTR gene".

With the second indication extension on 5 January 2022, Trikafta can now also be used for the treatment of patients aged 6 years and older with cystic fibrosis who have at

least one F508del mutation in the "CFTR gene".

Cystic fibrosis 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, although not all mutations of the CFTR gene lead to illness with symptoms of 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 on each chromosome of the double set 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.

¹ Chromosomes: Chromosomes are the carriers of genetic information and are located in the cell nuclei

² CFTR: Cystic Fibrosis Transmembrane Conductance Regulator

Since this is a rare and life-threatening disease, the medicine has been authorised as an

orphan drug. "Orphan drug" is a designation given to important medicinal products 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 number of 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"³, although these are very rare in Switzerland.

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 the CFTR protein in F508del defects. However, the underlying genetic defect is not cured.

Use

Trikafta is available on prescription only and contains different film-coated tablets (morning dose and evening dose). The morning dose contains elexacaftor, tezacaftor and ivacaftor. The active substances are combined in a single tablet. The evening dose only contains ivacaftor. The dosage is adjusted according to the patient's age and weight.

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 cystic fibrosis patients who had an F508del defect on two 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 106, Part B, was particularly important

³ 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.

for evaluating efficacy. This study investigated cystic fibrosis patients aged between 6 and 11 who had an F508del defect on two chromosomes or an F508del defect on one chromosome and an MF mutation ("minimal function mutation") on the second chromosome. The study participants were seriously ill and all weighed 15 kg or more. The median⁴ age of the patients was 9.3 years. Those participants who weighed less than 30

kg received half of the standard dosage for patients aged 12 years or older. Patients who already weighed 30 kg or more received the standard dosage.

The results were evaluated after a treatment period lasting 24 weeks. The treatment with Trikafta produced a statistically significant improvement in lung function compared to the start of treatment.

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 ab-

dominal pain, diarrhoea, increased liver enzymes (sign of stress on the liver) or a change in the bacterial species 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 106 shows that Trikafta is also beneficial in children aged 6 years and older with cystic fibrosis and F508del defects on just one chromosome and a second mutation on the other chromosome.

Taking into account all the risks and precautions, and on the basis of the available data,

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 6 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 can answer any further questions.

⁴ Median: The value that lies exactly in the middle of a distribution of data is called the median or central value. Half of

the data values are always smaller than the median, the other half are always greater.

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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