swissmedic

Summary report on authorisation dated 11 December 2024

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

Indication extension in Switzerland: 13 June 2024

Medicine (granules in sachet) 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 a so-called F508del mutation (defect) on 2 chromosomes[1] or an F508del mutation on 1 chromosome together with a defect on the second chromosome that prevents the formation of a functional *CFTR*[2] *protein* (so-called "minimal function mutation").

On 14 September 2021, the authorised indication for Trikafta was extended so that patients aged 12 years and older with cystic fibrosis and an F508del mutation could be treated regardless of the mutation on the second chromosome. On 5 January 2022, a further indication extension was approved for the treatment of patients aged 6 years and older.

With the third indication extension, approved by Swissmedic on 13 June 2024, Trikafta can now also be used for the treatment of patients aged 2 years and older with cystic fibrosis who have at least 1 F508del mutation in the CFTR gene.

Cystic fibrosis is a genetic disease caused by a deficiency and/or a dysfunction of the CFTR gene. The CFTR gene controls the formation (coding) of a protein used for transporting water and salts. The CFTR protein is also termed a chloride channel and sits on the cell surface. Chloride can move out of the cell through the channel. A dysfunction of the CFTR protein can lead, for example, to the formation of thick mucus in the lungs or pancreas, as well as elevated chloride levels in sweat.

Various mutations 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

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

[2] CFTR: Cystic Fibrosis Transmembrane Conductance Regulator

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.

Since cystic fibrosis with the F508del mutation in the CFTR gene is a rare, life-threatening disease, the indication extension has been authorised for the medicinal product Trikafta as an orphan drug. The term "orphan drug" is used to refer to important medicines for rare diseases.

Mode of action

The active substances tezacaftor and elexacaftor contained in Trikafta are so-called CFTR correctors, which bind to various sites on the CFTR protein, enabling them to improve the formation and the transport of CFTR proteins to the cell surface. The active substance ivacaftor helps improve the function of the CFTR channel at the cell surface.

The combination of the 3 active substances, elexacaftor, tezacaftor, and ivacaftor improves the function, and increases the quantity of, the CFTR protein in F508del defects at the cell surface, thereby increasing CFTR activity.

Thanks to the mechanism of action of these 3 combined active substances, the medicinal product Trikafta alleviates the symptoms associated with cystic fibrosis.

However, the underlying genetic defect is not cured.

Use

Trikafta is available on prescription only. For the indication extension for the treatment of patients aged 2 years and older, Trikafta is available as granules in sachets (morning dose and evening dose).

The morning and evening doses are each available in 2 dosage strengths:

Morning dose

- Sachet containing 80 mg of elexacaftor, 40 mg of tezacaftor, and 60 mg of ivacaftor
- Sachet containing 100 mg of elexacaftor, 50 mg of tezacaftor, and 75 mg of ivacaftor

Evening dose

- Sachet containing 59.5 mg of ivacaftor
- Sachet containing 75 mg of ivacaftor

The doctor will prescribe the dosage based on the patient's age and weight.

The morning and evening doses should be taken approximately 12 hours apart.

The entire contents of the sachet should be mixed with 5 ml of age-appropriate soft food or liquid and the mixture consumed immediately. A fat-containing meal or snack should be taken before or after the dose.

Efficacy

For the requested indication extension, study 445-111 was particularly important for evaluating efficacy. This study investigated 75 patients aged 2 to less than 6 years with cystic fibrosis.

The results were evaluated after a treatment period lasting 24 weeks. The study was not blinded and did not include a placebo control group[3].

[3] Placebo: dummy drug

The study showed that the treatment with Trikafta significantly improved the sweat chloride level and lung function in patients aged 2 to less than 6 years compared to the start of treatment.

The efficacy of Trikafta in patients with cystic fibrosis aged 2 to less than 6 years is supported by evidence from studies with Trikafta in patients aged 12 years and older.

Precautions, undesirable effects, & risks

Trikafta may not be used in those who are hypersensitive to 1 of the active substances or any of the excipients.

The most common side effects of Trikafta (affecting more than 1 in 10 users) are cough, fever, runny nose, nasal congestion, vomiting, rash, upper respiratory tract infections, loss of appetite, and increased liver enzymes (signs of stress on the liver).

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

Why the medicinal product has been authorised

Although medicinal products are already authorised for the treatment of cystic fibrosis, there is a need for effective and safe medicines for the treatment of children aged between 2 and 6 years suffering from cystic fibrosis with an F508del defect in the CFTR gene.

The submitted additional study 445-11 showed the benefit of Trikafta in children with cystic fibrosis aged 2 years and older with the described gene defect.

Taking into account all the risks and precautions, and on the basis of the available data, Swissmedic has therefore authorised the medicinal product Trikafta, containing the active substances elexacaftor, tezacaftor, and ivacaftor, in Switzerland for the treatment of patients aged 2 years and older.

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.

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 Summary report on authorisation.

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