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Alyftrek (*deutivacaftor / tezacaftor / vanzacaftor*)

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

What is Alyftrek and what is it used for?

Alyftrek is a medicine used in people aged 6 years and older to treat cystic fibrosis, an inherited disease that has severe effects on the lungs, the digestive system and other organs.

Cystic fibrosis can be caused by various mutations (changes) in the gene that contains instructions for making a protein called 'cystic fibrosis transmembrane conductance regulator' (CFTR).

Mutations in the *CFTR* gene are grouped into five different classes (class I to class V) based on the problems they cause with the production of the CFTR protein. Alyftrek is used in people whose cystic fibrosis is caused by at least one mutation that is not a class I mutation. Class I mutations are mutations that result in no CFTR protein being produced.

Cystic fibrosis is rare, and Alyftrek was designated an 'orphan medicine' (a medicine used in rare diseases) on 12 November 2021. Further information on the orphan designation can be found on the EMA website.

Alyftrek contains the active substances deutivacaftor, tezacaftor and vanzacaftor.

How is Alyftrek used?

Alyftrek can only be obtained with a prescription. It should only be prescribed by healthcare professionals with experience in the treatment of cystic fibrosis.

Alyftrek is available as tablets taken by mouth once daily with foods containing fat. The dose depends on the patient's body weight. The dose of Alyftrek may need to be reduced 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, as they may affect the way Alyftrek works in the body.

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

How does Alyftrek work?

Cystic fibrosis is caused by mutations in the CFTR gene. This gene leads to the production of the CFTR protein, which works on the surface of cells to regulate the production of mucus in the lungs and

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digestive juices in the gut. The mutations reduce the number of CFTR proteins on the cell surface or affect the way the protein works, resulting in mucus and digestive fluids being too thick, which leads to blockages, inflammation, increased risk of lung infections, and poor digestion and growth.

Two of the active substances in Alyftrek, vanzacaftor and tezacaftor, increase the number of CFTR proteins on the cell surface, while the other, deutivacaftor, improves the activity of the defective CFTR protein. These actions combine to make lung mucus and digestive juices less thick, thereby helping to relieve symptoms of the disease.

What benefits of Alyftrek have been shown in studies?

Alyftrek was as effective as another medicine, Kaftrio, at improving lung function in two main studies in people aged 12 years and older with cystic fibrosis. Kaftrio, which contains ivacaftor, tezacaftor and elexacaftor, is always given together with a medicine containing ivacaftor alone. Kaftrio is used in people with cystic fibrosis caused by at least one mutation that is not a class I mutation in the *CFTR* gene.

In both studies participants above 12 years of age received treatment with Kaftrio for four weeks and were then given either Alyftrek or continued treatment with Kaftrio. The main measure of effectiveness in both studies was the change in ppFEV1, which is the maximum amount of air a person can breathe out in one second compared with values from an average person with similar characteristics (such as age, height and sex). A normal ppFEV1 is typically close to 100 percentage points when the lungs are working properly.

The first study involved 405 participants with an *F508del* mutation and a 'minimal function' mutation. Minimal function mutations produce (almost) no CFTR protein or a defective CFTR protein that is not responsive to CFTR modulators. Following the first 4 weeks of treatment with Kaftrio, patients in the study had an average ppFEV1 of 67.1 percentage points. After 24 weeks of treatment, ppFEV1 was maintained both in participants given Alyftrek and those given Kaftrio.

The second study involved 573 participants with and without an *F508del* mutation. Those without an *F508del* mutation had at least one mutation that responded to treatment with Kaftrio. Following the first 4 weeks of treatment with Kaftrio, participants in the study had an average ppFEV1 of 66.8 percentage points. After 24 weeks of treatment, ppFEV1 was maintained both in participants given Alyftrek and those given Kaftrio.

The company also presented data from a study involving 78 children aged from 6 to 11 years with cystic fibrosis caused by at least one mutation responsive to treatment with Kaftrio. The study did not compare Alyftrek with another medicine or placebo (a dummy treatment). Data from the study showed that Alyftrek works in the same way in children aged 6 to 11 years as it does in older children and adults. Additionally, the effect of Alyftrek on lung function in children aged 6 to 11 years was generally consistent with that seen in older children and adults in the two main studies.

What are the risks associated with Alyftrek?

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

The most common side effects with Alyftrek (which may affect more than 1 in 10 people) include headache and diarrhoea. Some side effects can be serious. The most frequent with Alyftrek (which may affect up to 1 in 100 people) include an increase in liver enzymes which may be a sign of problems with the liver.

Why is Alyftrek authorised in the EU?

Alyftrek was shown to be at least as effective as Kaftrio for the treatment of people with cystic fibrosis. Alyftrek's safety profile is similar to that of Kaftrio; no new safety concerns were identified with Alyftrek. However, there are limited data on the long-term safety, particularly in children. The European Medicines Agency decided that Alyftrek's benefits are greater than its risks and that it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Alyftrek?

The company that markets Alyftrek will carry out a study based on a patient registry to provide further data on the safety and effectiveness of Alyftrek in people with cystic fibrosis caused by at least one mutation that is not a Class I mutation.

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

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

Other information about Alyftrek

Alyftrek received a marketing authorisation valid throughout the EU on 30 June 2025.

Further information on Alyftrek can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/alyftrek.

This overview was last updated in 06-2025.