



DRUG SAFETY UPDATE (DSU)

Kaftrio ▼ (Ivacaftor, tezacaftor, elexacaftor): risk of psychological side effects

Specialisms: Respiratory disease and allergy, General practice, Pharmacy

Summary

Psychological side effects such as anxiety, low mood, sleep disturbance, poor concentration, and forgetfulness have been infrequently reported in people with cystic fibrosis treated with Kaftrio. Healthcare professionals should advise patients and their caregivers that, while the risk is small, they should be alert to changes in mood and behaviour and, if they occur, to seek medical advice as soon as possible.

Advice for Healthcare Professionals:

- there is a small increase in the risk of psychological side effects in people with cystic fibrosis treated with Kaftrio
- there is also an indirect risk of psychological side effects from difficulty adjusting to Kaftrio-related improvements to physical health and quality of life
- individuals with life-limiting conditions such as cystic fibrosis also have an increased background risk of developing poor mental health
- advise patients and their caregivers to be alert to the development of psychological side effects usually within the first three months of treatment including anxiety or low mood, sleep disturbance, poor concentration, or forgetfulness. The side effects may occur in people who have no history of these problems.
- in some children, the psychological side effects may manifest themselves as persistent changes in behaviour while taking Kaftrio. Signs of this could include being more disruptive or difficult to manage
- discuss the benefit-risk balance of Kaftrio treatment with the patient or caregiver and consider treatment discontinuation if a patient develops these symptoms
- report suspected adverse drug reactions associated with Kaftrio on a [Yellow Card](#)

Advice for Healthcare Professionals to Provide to Patients:

- Kaftrio is a medicine used for the treatment of cystic fibrosis

- there have been infrequent reports in patients of all ages of low or altered mood, anxiety, problems with sleep, concentration, and/or forgetfulness
- some children, while taking Kaftrio, may notice persistent changes in the way they feel and/or act that are different to their usual patterns. This includes being more disruptive or difficult to manage
- these events usually happen within the first three months after starting treatment with Kaftrio and may occur in people who have no history of these problems
- it can be difficult for patients to know if their symptoms relate to Kaftrio or to something else. For some people, these changes can be associated with adjusting to the improvements that Kaftrio has on their physical health and their quality of life
- for many, the symptoms may not last long, but others will continue to experience them whilst they take Kaftrio.
- you may not notice some changes in your mood and behaviour so it is very important to tell your friends and family that you are taking this medicine and that it can have psychological side effects. Others may notice changes and help you quickly identify any symptoms that you need to talk to your doctor about
- talk to your doctor or cystic fibrosis team as soon as possible if you or your family or friends notice signs or symptoms of psychological side effects. Your doctor will advise on the most appropriate action to take
- report suspected adverse drug reactions associated with Kaftrio on a [Yellow Card](#)

Background

Review of adverse psychological side effects with Kaftrio

Adults and children with chronic diseases including cystic fibrosis are at an increased risk of experiencing adverse psychological effects. In addition, individuals with cystic fibrosis who experience marked improvements in wellness related to their cystic fibrosis may sometimes have difficulty in adjusting to the benefits of Kaftrio¹.

The Cystic Fibrosis Trust shared with the MHRA a suspected risk of adverse psychological effects during treatment with Kaftrio. This included reports of anxiety or low mood, sleep disruption, disturbances in concentration, and forgetfulness. It also included reports of persistent changes in behaviour in children while taking Kaftrio. These events frequently occurred within the first three months after starting treatment. The MHRA reviewed the available evidence for the risk, including experiences and insights provided by representatives from the cystic fibrosis community and the Cystic Fibrosis Trust. The review sought independent expert advice from the Commission on Human Medicines (CHM). The CHM advised that there is a small increase in the risk of developing adverse psychological effects during treatment with Kaftrio in a minority of people with cystic fibrosis. This risk may be associated with the medication itself but it could also be related to patients adjusting to improvements that Kaftrio has on their physical health and their quality of life. The CHM advised that healthcare professionals should discuss the benefit-risk balance of Kaftrio treatment with the patient or caregiver and consider treatment discontinuation if a patient develops these symptoms.

Updated product information for patients and healthcare professionals

Information to describe the risk will be added to the Kaftrio [Summary of Product Characteristics \(SmPC\)](#) and [Patient Information Leaflet \(PIL\)](#) in the UK. The updates will include a warning on the risk of side effects on mood, sleep, concentration and behaviour and advise that patients and caregivers should be advised to monitor for these symptoms. The product information will also advise that patients or carers of patients taking Kaftrio must contact their healthcare professional as soon as possible if the patient experiences these side effects.

Other cystic fibrosis modulators

Advice from independent experts is that there is insufficient evidence to indicate an increased risk of adverse psychological side effects with other cystic fibrosis modulators currently approved in the UK which were considered by this review ([Kalydeco](#), [Orkambi](#) and [Symkevi](#)).

UK reports of adverse psychological effects with Kaftrio

Up to 25 February 2025, the MHRA received 300 Yellow Card reports of suspected adverse psychological side effects in patients treated with Kaftrio. This is in the context of a total of 9391 people in the UK who have taken Kaftrio by 10 January 2025. It is not possible to determine the frequency of these events from the currently available data. Some patients affected had no medical history of mental health issues.

About Kaftrio

Kaftrio belongs to a class of medicines known as cystic fibrosis modulators which target the underlying defective protein in cystic fibrosis, restoring normal protein function in the lung and other organs. Kaftrio is indicated in a combination regimen with ivacaftor (Kalydeco) for the treatment of cystic fibrosis in patients aged 2 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator gene. The F508del mutation is the most common mutation in the cystic fibrosis transmembrane conductance regulator gene, found in more than 80% of people of Northern European descent with cystic fibrosis.

Reporting advice

Healthcare professionals, patients, and caregivers are asked to submit reports using the Yellow Card scheme electronically using:

- the [Yellow Card website](#).
- the Yellow Card app; download from the [Apple App Store](#) or [Google Play Store](#)
- some clinical IT systems for healthcare professionals (EMIS, SystmOne, Vision, MiDatabank, and Ulysses)

When reporting suspected adverse drug reactions, please provide as much information as possible, including information about medical history, any concomitant medication, onset timing, and treatment dates.

Additional information

You can [sign up](#) to receive email notifications for Drug Safety Updates.

You can [sign up](#) to receive our monthly roundup of safety communications.

For any enquiries, please contact info@mhra.gov.uk

References

1. [Kaftrio - complex and individual experiences.pdf \(cysticfibrosis.org.uk\)](#), Cystic Fibrosis Trust, March 2022

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