Medicines & Healthcare products Regulatory Agency

MHRA SAFETY ROUNDUP

May 2025

Summary of the latest safety advice for medicines and medical device users

Contents

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Thiopurines and intrahepatic cholestasis of pregnancy

Access the full article

Specialisms: *GI, hepatology and pancreatic disorders, rheumatology, dermatology, haematology and oncology, immunosuppression and transplantation, obstetrics, gynaecology and fertility, pregnancy, cancer.*

Summary

Intrahepatic cholestasis of pregnancy (ICP) has been rarely reported in patients treated with azathioprine products and is believed to be a risk applicable to all drugs in the thiopurine class (azathioprine, mercaptopurine and tioguanine). Cholestasis of pregnancy associated with thiopurines tends to occur earlier in pregnancy than non drug-induced cholestasis of pregnancy, and elevated bile acid levels may not reduce with ursodeoxycholic acid.

Key Advice for Healthcare Professionals:

- cholestasis of pregnancy has rarely been reported in association with azathioprine therapy
- this risk is believed to also apply to the other thiopurine drugs, mercaptopurine and tioguanine
- it may occur earlier in pregnancy than non drug-induced cholestasis of pregnancy, and it may not respond to ursodeoxycholic acid
- withdrawal or dose reduction of the thiopurine drug may improve liver function tests
- remain vigilant to signs and symptoms of ICP in pregnant patients taking thiopurines and discuss any concerns with clinicians managing the patient's immunosuppressant therapy and a hepatologist, as necessary
- if cholestasis of pregnancy occurs, a case-by-case assessment is required to determine the appropriate course of action. Consider the risks and benefits of remaining on the product against the risks and benefits of stopping.
- in patients with ICP, measure serum bile acids to identify pregnancies at particular risk of spontaneous preterm birth (≥40uM) or stillbirth (non-fasting serum bile acids ≥100uM)

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Key Advice for Healthcare Professionals to Provide to Patients:

- talk to your doctor or midwife immediately if you experience symptoms of cholestasis of pregnancy which include intense itching without a rash, nausea, and loss of appetite
- do not stop taking your medication unless advised to do so by your doctor or midwife

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

Access the full article

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.

Key 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

Key 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

Letters, medicines recalls and device notifications sent to healthcare professionals in April and May 2025

Direct Healthcare Professional Communications

In April and May 2025, the following Direct Healthcare Professional Communications were sent or provided to relevant healthcare professionals:

- ACCUSOL 35 Potassium 4 mmol/L solution for haemofiltration (BWPE04): labelling defect
- Accord-Healthcare Limited is currently experiencing supply disruption with Sondelbay (teriparatide) 20mcg/80mcl solution for injection in a pre-filled pen in the UK

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- BD ChloraPrep™ Clear - 1mL Applicator: Recall of affected batches due to packaging defect and subsequent risk of contamination
- Erelzi (etanercept) 50 mg solution for injection in pre-filled pen Interim Supply of Irish Stock

Medicine Recalls and Notifications

In May 2025, recalls and notifications for medicines were issued on:

Class 2 Medicines Recall: Mercaptopurine 50mg Tablets, Aspen Pharma Trading Limited, EL (25)A/23. Issued 22 May 2025

Aspen Pharma Trading Limited is recalling a specific batch of Mercaptopurine 50mg tablets as a precautionary measure due to microbial contamination following a small number of complaints of discoloured tablets within the packs, identified when the packs have been opened by healthcare professionals.

Class 2 Medicines Recall: BD ChloraPrep Clear - 1mL Applicator, Becton Dickinson UK Ltd, EL(25)A/22. Issued 19 May 2025

Becton Dickinson UK Ltd has informed the MHRA that some units exhibit an open seal on the packaging of the applicator. This defect could increase the risk of the applicator device being contaminated with pathogens, which could lead to increased infection rates for the patients.

Class 4 Medicines Notification: Chemidex Pharma Ltd, Various Products, EL(25)A/21. Issued 13 May 2025

Chemidex Pharma Ltd has informed the MHRA that the Patient Information Leaflet (PIL) in their topical steroid products does not contain all the required safety information. Cartons for the products/batches listed are missing side effect information related to Visual Disturbances.

Class 4 Medicines Defect Notification: Chloramphenicol 1% w/w Eye Ointment, Blumont Pharma Limited, EL(25)A/20. Issued 8 May 2025

Blumont Pharma Limited has informed the MHRA of an error with the European Article Number (EAN) barcode on the cartons of the batch of Chloramphenicol 1% w/w Eye Ointment (POM version only).

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Medical Device Field Safety Notices

Find recently published Field Safety Notices

Report suspected drug reactions and device incidents on a Yellow Card

Please continue to report suspected adverse drug reactions and device incidents. Your report will help us safeguard public health.

When reporting, please provide as much information as possible, including information about medical history, any concomitant medication, onset timing, treatment dates and particularly if a side effect continued or started after treatment was stopped.

Report a medicine

Healthcare professionals should report via a Yellow Card to:

- 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)

Reporting for medical devices

Healthcare professionals should report incidents:

- in England and Wales to the Yellow Card website or via the Yellow Card app
- in Scotland to Incident Reporting & Investigation Centre (IRIC) and their local incident recording system
- in Northern Ireland to the Northern Ireland Adverse Incident Centre and their local incident recording system

Reporting for Patients

Report a medicine or medical device

Patients should report via a Yellow Card to:

- the Yellow Card website
- the Yellow Card app; download from the Apple App Store or Google Play Store

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News Roundup

Update to the Core SmPC and Package Leaflet for Hormone Replacement Products (HRT) products

Please be aware of an upcoming update to the Summary of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for Hormone Replacement Therapy (HRT) products. The update highlights the interaction between oestrogens and the following direct-acting antiviral agents (DAAs) used for the treatment of hepatitis C virus (HCV) infection, which in some clinical trials have been linked to alanine transaminase (ALT) elevations:

- sofosbuvir/velpatasvir/voxilaprevir
- ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin

Healthcare professionals are advised to make themselves aware of the potential for drug interactions with the additional HCV combination drug regimens included in the update and to review patients' medications where necessary. For further details on these updates, please see the Co-ordination Group for Mutual Recognition and Decentralised procedures - Human (CMDh) website under Product information > Core SmPC/PL. Please find a link to the tracked changed version of the SMPC (refer to pages 7 & 8).

Be aware of the potential for Biotin interference on thyroid function laboratory tests

Biotin, also known as vitamin B7, is a water-soluble vitamin often found in multi-vitamins and dietary supplements marketed for hair, skin, and nail growth. Biotin may interfere with thyroid immunoassays and the risk of interference increases with higher doses of biotin.

Healthcare professionals should ask adults, children and young people with suspected thyroid dysfunction about their biotin intake because a high consumption of biotin may lead to falsely high or low test results.

MHRA launches consultation on the use of real-world data for external control arms of clinical trials

The MHRA is launching a six-week consultation on a draft guideline for the use of real-world data for external control arms of clinical trials, which has the potential to help accelerate the approval of treatments, especially in cases when randomised controlled trials may not be ethical or feasible. Real-world data refers to information that is collected from patients during the course of their normal clinical care. A control arm of the study would use data from patients not part of a specific clinical trial.

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