



Latest advice for medicines users

The monthly newsletter from the Medicines and Healthcare products Regulatory Agency and its independent advisor the Commission on Human Medicines

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The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for ensuring that medicines and medical devices work and are acceptably safe.

The Commission on Human Medicines gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.



NICE has accredited the process used by the MHRA to produce Drug Safety Update guidance. More information on accreditation can be viewed on the [NICE website](https://www.nice.org.uk/accreditation).

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Our first article reminds healthcare professionals prescribing fluoroquinolone antibiotics (ciprofloxacin, delafloxacin, levofloxacin, moxifloxacin, ofloxacin) to be alert to the risk of disabling and potentially long-lasting or irreversible side effects.

We also remind that fluoroquinolone treatment should be discontinued at the first signs of a serious adverse reaction, including tendon pain or inflammation.

Next, we remind prescribers to advise patients receiving methotrexate to take precautions in the sun to avoid photosensitivity reactions. Photosensitivity reactions are known side effects of methotrexate treatment and can be severe. See the article on page 6 for advice that can be provided to patients and caregivers.

On page 9 we provide an update on a retrospective observational study on the risk to children born to men who took valproate in the 3 months before conception and on the need for the re-analysis of the data from this study before conclusions can be drawn.

Our final article provides a summary of recent letters and notifications sent to healthcare professionals about medicines. If you have been forwarded this issue of Drug Safety Update, [subscribe directly via our website](#).

Fluoroquinolone antibiotics: reminder of the risk of disabling and potentially long-lasting or irreversible side effects

Healthcare professionals prescribing fluoroquinolone antibiotics (ciprofloxacin, delafloxacin, levofloxacin, moxifloxacin, ofloxacin) are reminded to be alert to the risk of disabling and potentially long-lasting or irreversible side effects. Do not prescribe fluoroquinolones for non-severe or self-limiting infections, or for mild to moderate infections (such as in acute exacerbation of chronic bronchitis and chronic obstructive pulmonary disease) unless other antibiotics that are commonly recommended for these infections are considered inappropriate. Fluoroquinolone treatment should be discontinued at the first signs of a serious adverse reaction, including tendon pain or inflammation.

Advice for healthcare professionals:

- systemic (by mouth, injection, or inhalation) fluoroquinolones can cause long-lasting (up to months or years), disabling, and potentially irreversible side effects, sometimes affecting multiple systems, organ classes, and senses
- despite [new restrictions and precautions](#) introduced in 2019, [a new study](#) has shown no evidence of a change in fluoroquinolone prescribing patterns in the UK, and the MHRA has continued to receive Yellow Card reports of these side effects
- advise patients to stop treatment at the first signs of a serious adverse reaction, such as tendinitis or tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy, and central nervous system effects, and to contact their doctor immediately for further advice – [sheet for patients](#)
- do not prescribe fluoroquinolones:
 - for non-severe or self-limiting infections, or non-bacterial conditions, for example non-bacterial (chronic) prostatitis
 - for mild to moderate infections (such as in acute exacerbation of chronic bronchitis and chronic obstructive pulmonary disease) unless other antibiotics that are commonly recommended for these infections are considered inappropriate (see below)
- do not prescribe ciprofloxacin or levofloxacin for uncomplicated cystitis unless other antibiotics that are commonly recommended are considered inappropriate (see below)
- avoid fluoroquinolone use in patients who have previously had serious adverse reactions with a quinolone antibiotic (for example, nalidixic acid) or a fluoroquinolone antibiotic
- prescribe fluoroquinolones with special caution for people older than 60 years and for those with renal impairment or solid-organ transplants, because they are at a higher risk of tendon injury
- avoid use of a corticosteroid with a fluoroquinolone since coadministration could exacerbate fluoroquinolone-induced tendinitis and tendon rupture
- report suspected adverse drug reactions to fluoroquinolone antibiotics on the [Yellow Card website](#) or via the Yellow Card app (download it from the [Apple App Store](#), or [Google Play Store](#))

Advice for healthcare professionals to provide to patients, parents and carers:

- fluoroquinolone antibiotics are a group of antibiotics that include ciprofloxacin, delafloxacin, levofloxacin, moxifloxacin, and ofloxacin – sometimes these medicines may also have a brand name so patients should check the details of all antibiotics prescribed to them
- fluoroquinolone antibiotics have been reported to cause serious side effects involving tendons, muscles, joints, nerves, or mental health – in some patients, these side effects have caused long-lasting or permanent disability
- stop taking your fluoroquinolone antibiotic and contact your doctor immediately if you have any of the following signs of a side effect:
 - tendon pain or swelling – if this happens, rest the painful area until you can see your doctor
 - pain in your joints or swelling in your shoulders, arms, or legs
 - abnormal pain or sensations (such as persistent pins and needles, tingling, tickling, numbness, or burning), weakness in your body, especially in the legs or arms, or difficulty walking
 - severe tiredness, depressed mood, anxiety, or problems with your memory or severe problems sleeping
 - changes in your vision, taste, smell, or hearing
- tell your doctor if you have had any of the above effects during or shortly after taking a fluoroquinolone – this means you should avoid them in the future

Disabling and potentially long-lasting or irreversible side effects

Systemic and inhaled fluoroquinolones are associated with a risk of serious, disabling, long-lasting and potentially irreversible adverse reactions. These may affect different, sometimes multiple, body systems, and may include musculoskeletal, nervous, psychiatric, and sensory reactions. They have been reported in patients irrespective of their age and risk factors. Tendon damage (including the Achilles tendon but other tendons can also be involved) can occur within 48 hours of commencing treatment, or the effects can be delayed for several months and become apparent after stopping treatment.

There are no pharmacological treatments established to be effective for these disabling and potentially long-lasting or irreversible side effects. However, it is important that these symptoms are appropriately investigated, and that fluoroquinolones are stopped immediately at the first signs or symptoms of a serious adverse reaction to avoid further exposure, which could potentially worsen adverse reactions.

[Restrictions to the use of fluoroquinolones](#) were introduced in 2019 to minimise the risk of these reactions.

Fluoroquinolones should not be prescribed for treatment of mild to moderate infections (such as in acute exacerbation of chronic bronchitis and chronic obstructive pulmonary disease) unless other antibiotics that are commonly recommended for these infections are considered inappropriate.

Relevant situations in which other antibiotics may be inappropriate are where:

- there is resistance to other first-line antibiotics recommended for the infection
- other first-line antibiotics are contraindicated in an individual
- other first-line antibiotics have caused side effects requiring treatment to be stopped
- treatment with other first-line antibiotics has failed

Further review by MHRA

After conducting a further review, the MHRA sought the advice of the Commission on Human Medicines (CHM) on existing the success of measures to minimise the risk of disabling and potentially long-lasting or irreversible side effects of fluoroquinolones. The MHRA review involved engagement with patients and patient representatives to seek their views. It also included a review of data from a new study of fluoroquinolone prescribing in 6 European countries, including the UK,¹ following the introduction of new restrictions for use, alongside data from other sources.

While the new study referenced above reported an overall decrease in the prescribing of fluoroquinolones in primary care in the UK, there was no evidence of a change in prescribing patterns as a result of the restrictions introduced in 2019. The study noted continued prescribing of fluoroquinolones in patients with risk factors for adverse reactions, such as patients who were concomitantly prescribed corticosteroids.

We also continue to receive Yellow Card reports of these side effects, including reports where a fluoroquinolone was prescribed in situations where the product information includes a warning, or where a fluoroquinolone was prescribed for a mild or moderate infection and where an alternative antibiotic may have been appropriate. The CHM advised that it would be important to increase awareness of these risks among healthcare professionals. We will communicate in due course any additional regulatory actions in the UK as a result of this review.

Report suspected reactions on a Yellow Card

Please continue to report suspected adverse drug reactions to the [Yellow Card scheme](#). Your report will help us safeguard public health. 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 please provide as much information as possible, including information about batch numbers, medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

References

1. Ly NF and others. [Impact of European Union Label Changes for Fluoroquinolone-Containing Medicinal Products for Systemic and Inhalation Use: Post-Referral Prescribing Trends](#). Drug Safety 2023; issue 46, pages 405 to 416.

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Methotrexate: advise patients to take precautions in the sun to avoid photosensitivity reactions

Photosensitivity reactions are known side effects of methotrexate treatment and can be severe. Patients should be advised to take precautions to protect their skin in the sun.

Advice for healthcare professionals:

- photosensitivity reactions (which include phototoxicity, where a drug is activated by exposure to UV light and causes damage to the skin that can look and feel like a sunburn or a rash) are known side effects of methotrexate treatment and can occur with both low-dose and high-dose treatment
- reactions manifest as severe sunburn such as rashes with papules or blistering, with some patients reporting swelling; rarely, photosensitivity reactions have contributed to deaths from secondary infections
- healthcare professionals, including those prescribing and dispensing methotrexate, should remind patients to take precautions to protect themselves from the sun and UV rays
- report suspected adverse drug reactions associated with methotrexate on a [Yellow Card](#)

Advice for healthcare professionals to provide to patients and caregivers:

- methotrexate treatment may make your skin more sensitive to the sun
- sun exposure during methotrexate treatment could cause very severe reactions that look and feel like sunburn
- avoid exposure to intense sunlight (especially between 11 am and 3 pm) or to UV rays (for example, using sunbeds or tanning equipment) while taking methotrexate
- use a sun protection product with a high protection factor when exposed to the sun
- wear a hat and clothes that cover your arms and legs when in the sun
- talk to a healthcare professional if you are worried about a skin reaction you have had while taking methotrexate

Review of photosensitivity reactions with methotrexate

Methotrexate is an immunosuppressant medicine that is used to treat inflammatory conditions such as rheumatoid arthritis, psoriasis, and Crohn's disease. It is also used as a cancer treatment.

The MHRA has recently received a Coroner's report following a case of a photosensitivity reaction in a patient on methotrexate.

This reaction was found to have contributed to their death by secondary infection. As a result of this, we have reviewed the information available to healthcare professionals and patients regarding these reactions and sought advice from the Pharmacovigilance Expert Advisory Group (PEAG) of the [Commission on Human Medicines](#).

Photosensitivity reactions are established side effects of methotrexate treatment and are currently listed in the product information, including the Patient Information Leaflet. However, the PEAG was concerned that it is not a well-known side effect and many patients may not be aware of the additional risks of sun exposure during methotrexate treatment.

Prescribers and pharmacists are reminded to inform patients of the risk of photosensitivity reactions and to advise them to use a product with a high sun protection factor and clothing that covers the skin when in the sun. We are working with Marketing Authorisation Holders of methotrexate medicines to provide updates to the product information as appropriate.

Characteristics of reactions

Photosensitivity reactions often look and feel like sunburn. They can leave sun-exposed skin with a rash, redness, swelling, blisters, red bumps or oozing lesions. Severe cases can cause secondary skin infection. Photosensitivity reactions fall into two categories; phototoxic reactions and photoallergic reactions.

In phototoxic reactions, a drug is activated by exposure to UV light and causes damage to the skin that can look and feel like a sunburn or a rash. These reactions can happen within minutes or after hours of exposure and are usually limited to the skin that has been exposed.

Photoallergic reactions occur when UV rays interact with the ingredients in medicines or other products applied directly to the skin. The body's immune system recognizes changes caused by sun exposure as a foreign threat. The body produces antibodies and attacks, causing a reaction.^{1, 2}

These reactions are distinct from "recall" reactions where radiation-induced dermatitis and sunburn can reappear on re-exposure to radiation and sunlight while on methotrexate therapy.

Report suspected reactions on a Yellow Card

Please continue to report suspected adverse drug reactions to the [Yellow Card scheme](#). 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, SystemOne, Vision, MiDatabank, and Ulysses)

When reporting please provide as much information as possible, including information about batch numbers, medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

References

1. Skin Cancer Foundation. [Photosensitivity & Your Skin](#). Accessed July 2023.
2. Glatz M, Hofbauer GFL. [Phototoxic and photoallergic cutaneous drug reactions](#). Chemical Immunology and Allergy 2012; volume 97: pages 167 to 179.

Article citation: Drug Safety Update volume 17, issue 1: August 2023: 2.

Valproate: re-analysis of study on risks in children of men taking valproate

We are providing an update on a retrospective observational study on the risk to children born to men who took valproate in the 3 months before conception and on the need for the re-analysis of the data from this study before conclusions can be drawn. No action is needed from patients.

It is vitally important that patients do not stop taking valproate unless they are advised by their specialist to do so.

For female patients, healthcare professionals should continue to follow the existing strict precautions related to preventing the use of valproate in pregnancy (Valproate Pregnancy Prevention Programme).

Advice for healthcare professionals:

- we continue to rigorously review all emerging data on valproate-containing medicines including findings from a retrospective observational study suggesting an increased risk of neurodevelopmental disorders in children whose fathers took valproate in the 3 months before conception, compared to those whose fathers took lamotrigine or levetiracetam
- however errors have been subsequently identified in the study that may impact on the results; a full re-analysis is required before conclusions can be drawn
- as soon as the revised study analysis is available, it will be carefully re-assessed by the MHRA, and any further guidance will be communicated to patients and healthcare professionals as soon as possible
- for female patients, continue to follow the existing strict precautions related to the known and significant harms of valproate in pregnancy (Valproate Pregnancy Prevention Programme, see page 11)
- GPs and pharmacists should continue to provide repeat prescriptions for valproate; patients currently taking valproate must be advised not to stop taking it unless they are advised by a specialist to do so
- report any suspected adverse drug reactions associated with valproate on a [Yellow Card](#)

Advice for healthcare professionals to provide to patients:

- valproate is a medicine for epilepsy and bipolar disorder; brand names of valproate include Convulex, Depakote, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell
- do not stop taking valproate or alter your dose without checking with your specialist first; if you stop taking valproate without your specialist's advice your condition may get worse
- valproate is associated with a significant risk of birth defects and neurodevelopmental disorders in children born to women who take valproate during pregnancy – see our [existing advice to women and girls](#)
- findings of a study submitted to the MHRA have suggested that there may be an increased risk of neurodevelopmental disorders in children of men who took valproate in the 3 months before conception in comparison to children born to men taking lamotrigine or levetiracetam
- however, errors have been identified in the study that may impact on the results; these mean a full re-analysis is being done before conclusions can be drawn
- as soon as the revised study analysis is available, it will be carefully re-assessed by the MHRA and any further guidance will be communicated to patients as soon as possible
- it is vitally important that you do not stop taking valproate unless a specialist tells you to; talk to a healthcare professional if you are concerned about your medicine or your or your child's health

Background

Valproate (as sodium valproate, valproate semisodium, or valproic acid) is authorised for use in epilepsy and bipolar disorder.

Valproate has a high teratogenic potential and children exposed in utero to valproate have a high risk for congenital malformations and neurodevelopmental disorders.

Valproate should not be prescribed to female children or women of childbearing potential unless other treatments are ineffective or not tolerated. Valproate is contraindicated in women of childbearing potential, unless the conditions of the pregnancy prevention programme are fulfilled – see Conditions of the valproate Pregnancy Prevention Programme below.

Clinicians prescribing in epilepsy should continue to [consult the findings of the epilepsy medicines in pregnancy review](#), particularly that lamotrigine (Lamictal) and levetiracetam (Keppra) were not associated with an increased risk of birth defects compared with the rate in the general population.

Valproate administration may also impair fertility in men. Fertility dysfunctions are in some cases reversible at least 3 months after treatment discontinuation, however in some cases the reversibility of male infertility was unknown. In addition, pre-clinical studies have reported adverse effects to the male reproductive system in juvenile and adult animals receiving valproate.

Re-analysis of study examining risk in children of men taking valproate

The MHRA has kept under close review the possibility of risks to children associated with paternal exposure to valproate (in other words, whether a child could be affected if a father was taking valproate). Two studies were conducted by researchers in 2013 that did not find evidence of an increased risk to children with paternal use of epilepsy medicines, but the studies had limitations.^{1,2} As part of the outcome of the [2018 European review of valproate](#), a new retrospective study was requested from the marketing authorisation holders to examine this risk.³

The study report submitted to the MHRA and to other regulatory authorities suggested an increased risk of neurodevelopmental disorders in children whose fathers took valproate during the 3-month period before they were conceived compared to children whose fathers had taken the antiseizure medicines lamotrigine or levetiracetam. However, we were subsequently informed of errors in the study that may impact on the results.

A full re-analysis is required before conclusions can be drawn. As soon as the revised study analysis is available, it will be re-assessed by the MHRA. No action is currently needed from patients. No one should stop taking valproate without advice from their specialist.

Reminder of the conditions of the valproate Pregnancy Prevention Programme

The prescriber must ensure that:

- individual circumstances are evaluated in each case, involving the patient in the discussion, to guarantee her engagement, discuss therapeutic options and ensure her understanding of the risks and the measures needed to minimise the risks
- the potential for pregnancy is assessed for all female patients
- the patient has understood and acknowledged the risks of congenital malformations and neurodevelopmental disorders including the magnitude of these risks for children exposed to valproate *in utero*
- the patient understands the need to undergo pregnancy testing prior to initiation of treatment and during treatment, as needed
- the patient is counselled regarding contraception, and that the patient is capable of complying with the need to use effective contraception, without interruption during the entire duration of treatment with valproate
- the patient understands the need for regular (at least annual) review of treatment by a specialist experienced in the management of epilepsy.
- the patient understands the need to consult her physician as soon as she is planning pregnancy to ensure timely discussion and switching to alternative treatment options prior to conception, and before contraception is discontinued

- the patient understands the need to urgently consult her physician in case of pregnancy
- the patient has received the [patient guide](#)
- the patient has acknowledged that she has understood the hazards and necessary precautions associated with valproate use ([Annual Risk Acknowledgement Form](#)).

These conditions also concern women who are not currently sexually active unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy.

Pharmacists should continue to ensure patients receive the patient card, a copy of the Patient Information Leaflet and packaging bearing pregnancy warnings.

References

1. Veiby G and others. [Exposure to antiepileptic drugs in utero and child development: a prospective population-based study](#). Epilepsia 2013: volume 54, pages 1462 to 1472.
2. Engeland A and others. [Effects of preconceptional paternal drug exposure on birth outcomes': cohort study of 340000 pregnancies using Norwegian population-based databases](#). British Journal of Clinical Pharmacology 2013: volume 75, pages 1134 to 1141.
3. European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCEPP). [Study protocol EUPAS34201](#) (accessed August 2023).

Article citation: Drug Safety Update volume 17, issue 1: August 2023: 3.

Letters and medicine recalls sent to healthcare professionals in July 2023

Letters

In July 2023, the following letters were sent or provided to relevant healthcare professionals:

- [Tibsovo ▼ 250 mg film coated tablets: Interim Supply of Irish packs to Mitigate Supply Disruption](#)
- [Rapifen Intensive Care 5mg/ml solution for injection \(10 x 2ml ampoules\): difficulty opening ampoules](#)
- [Systemic and inhaled fluoroquinolone antibiotics – reminder on restrictions of use](#)
- [Co-amoxiclav powder for oral suspension \(amoxicillin, clavulanic acid\), Amoxicillin Suspension \(amoxicillin\): wrong 'sugar free' label on outer package](#)

Medicine Recalls and Notifications

In July 2023, recalls and notifications for medicines were issued on:

[Class 3 Medicines Recall: Strandhaven Limited T/A Somex Pharma, Sildenafil 100mg Film-coated Tablets, EL\(23\)A/21](#). Issued 3 July 2023. Strandhaven Limited T/A Somex Pharma has informed the MHRA that the pack size on some cartons of the batch in this notification state 8 tablets instead of 4 tablets. This is an error due to cartons being mixed at the printers. Stop supplying and quarantine any stock with this batch number that is labelled as containing 8 tablets. The packs labelled as 4 tablets can be dispensed as normal.

[Class 2 Medicines Recall: medac GmbH \(t/a medac Pharma LLP\), Dacarbazine 100mg, 200mg & 500mg powder for solution for injection vials, EL\(23\)A/22](#). Issued 4 July 2023. medac GmbH (t/a medac Pharma LLP) is recalling the products and respective batches in this notification due to pink discolouration of the dacarbazine solution immediately after reconstitution (after correct preparation and storage). The pink discolouration is caused by a degradation product of dacarbazine and may cause a venous irritation in the patient when the product is applied. As stated in the Summary of Product Characteristics (SmPC), the diluted solution for infusion should be visually inspected and only clear solutions practically free from particles should be used. Do not use the solution if particles are present. Stop supplying the above batches immediately. Quarantine all remaining stock and return it to your supplier using your supplier's approved process.

[Class 2 Medicines Recall: Tillomed Laboratories Limited, Labetalol 200mg Tablets, EL\(23\)A/23](#). Issued 10 July 2023. Tillomed Laboratories Limited is recalling one batch of Labetalol 200mg Tablets due to an error on the foil blister packaging. The incorrect aluminium foil blister packaging states Labetalol 100mg Tablets, however it should be labelled as Labetalol 200mg Tablets. Stop supplying the affected batches immediately. Quarantine all remaining stock and return it to your supplier using your supplier's approved process.

[Class 4 Medicines Notification, Cipla \(UK\) Limited and Pharmathen S.A., Various Products, EL\(23\)A24](#). Issued 12 July 2023. Cipla (EU) Limited, UK has informed the

MHRA that the outer carton (box) of the product batches mentioned in this notification are missing the medicines legal classification for a Prescription Only Medicine 'POM.' Exercise caution when handling the listed products and ensure that they are stored accordingly and in line with the guidance for the storage of Prescription Only Medicines (POM). Only dispense these products when the pharmacy team receives a suitable prescription prescribed by a qualified health professional.

[Class 2 Medicines Recall: Aventis Pharma Limited \(t/a Sanofi\), Sabril 500 mg film-coated tablets & Sabril 500 mg granules for oral solution, EL\(23\)A/25.](#) Issued 13 July 2023.

Sanofi UK is recalling the listed batches of Sabril tablets and Sabril granules as a precautionary measure due to the detection of traces of tiapride in the batches of the source material. Stop supplying the above batches immediately. Quarantine all remaining stock and return it to your supplier using your supplier's approved process. All patients should be advised not to discontinue Sabril tablets or Sabril granules without consulting with their prescriber. The risks of suddenly stopping medication for seizures/epilepsy is higher than the potential risk presented by the presence of tiapride.

[Company led medicines recall: Quantum Pharmaceutical, Diltiazem HCl 2% Cream \[unlicensed medicine\], CLMR \(23\)A/05.](#) Issued 19 July 2023. Quantum Pharmaceutical

has informed the MHRA that the consistency of the product within the batches mentioned in this notification has changed. The product has a reduced viscosity and more closely resembles a lotion than a cream. Stop supplying the batches above immediately. Quarantine all remaining stock and liaise with Quantum Pharmaceutical on the return process. Quantum Pharmaceuticals has full traceability and will contact pharmacy teams that have been provided the affected products.

[Class 2 Medicines Recall: medac GmbH \(t/a medac Pharma LLP\), Sodiofolin 50 mg/ml solution for injection/infusion \(400mg/8ml vial\), EL \(23\)A/26.](#) Issued 20 July 2023. medac GmbH (t/a medac Pharma LLP) is recalling the products and respective batches in this notification due to particles detected during long-term stability tests. As stated in the Summary of Product Characteristics (SmPC): 'Only clear solutions without visible particles should be used'. These batches are being recalled as a precautionary measure and the root cause investigation remains ongoing. Stop supplying the affected batches immediately. Quarantine all remaining stock and return it to your supplier using your supplier's approved process.

[Class 2 Medicines Recall: B. Braun Medical Ltd, Various Products, EL\(23\)A/27.](#) Issued 31 July 2023. B. Braun Medical Limited is recalling various product batches as a precautionary measure after traces of midazolam were detected in the batches listed in this notification. A toxicological assessment has been completed to evaluate the potential risk for patients. The assessment concluded that the highest detected levels of midazolam are deemed to display no clinical effects. Nevertheless, although at low risk, allergic reactions to Midazolam cannot be excluded. B. Braun Medical Limited has not received any reports of suspected adverse drug reactions for the affected batches. Stop supplying the listed batches immediately. Quarantine all remaining stock and return it to your supplier using your supplier's approved process. Based on the distribution dates, most of the affected stock will have been used already. B. Braun has confirmed that other stock which is not impacted remains available.

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