Medicines & Healthcare products Regulatory Agency

Drug Safety Update

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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Contents

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.

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This month, we inform healthcare professionals that review by two specialists remains in place for patients initiating valproate under 55 years of age but the Commission on Human Medicines (CHM) has advised that it will not be required for men (or males) currently taking valproate.

Finally, we provide a summary of recent letters and notifications sent to healthcare professionals about medicines and medical devices.

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Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell▼): review by two specialists is required for initiating valproate but not for male patients already taking valproate

Review by two specialists remains in place for patients initiating valproate under 55 years of age but the Commission on Human Medicines (CHM) has advised that it will not be required for men (or males) currently taking valproate. Three infographics have been developed to provide clarity regarding valproate prescribing.

Advice for Healthcare Professionals:

- the CHM has advised that a review by two specialists is required for initiating valproate in patients under 55 years of age but not for men who are already taking valproate
- three infographics have been produced to clarify in which situations review by two specialists may be required:
  - for female patients under 55 years old
  - for male patients under 55 years old
  - for male and female patients 55 years and older
- a list of who might qualify as a specialist can be found at Valproate safety measures
- report suspected adverse reactions associated with valproate on Yellow Card

Reminder of previous advice for healthcare professionals:

Patients under 55 years of age starting valproate

- valproate must not be started in new patients (male or female) younger than 55 years unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply. For many patients, other effective treatment options are available to treat their bipolar disorder or epilepsy
- information on permanent reasons or compelling reasons as to why the reproductive risks may not apply to a patient may be sought from clinical guidance

Women and girls of childbearing potential currently taking valproate

- at their next annual specialist review, women and girls of childbearing potential receiving valproate should have their treatment reviewed using the revised Annual Risk Acknowledgement Form. At this review, if the patient has never been reviewed by two specialists either at initiation or annual review, a second specialist signature will be needed if the patient is to continue on valproate. Women do not need to be recalled for an additional review. Once a patient has received a treatment review by two specialists, subsequent annual reviews only require one specialist

Men currently taking valproate

- as a precaution, recommend that male patients and their female sexual partner use effective contraception (condoms, plus effective contraception used by female sexual partner) throughout the valproate treatment period and for 3 months after stopping valproate, to allow for one completed sperm cycle not exposed to valproate

- at their next regular treatment review, discuss with men on oral valproate treatment whether they are planning to father a child in the next year and if they are, refer to a specialist to discuss most appropriate treatment options
- advise men not to donate sperm during valproate treatment and for 3 months after stopping valproate
- if a female reports they are pregnant or planning a pregnancy with a man on valproate, refer them for prenatal counselling

Advice for Healthcare Professionals to Provide to Patients:

- do not stop taking valproate without advice from a specialist. This is because epilepsy or bipolar disorder may worsen without treatment
- if you are on valproate, please attend any offered appointments to discuss your treatment and talk to a healthcare professional if you are concerned
- if you wish to discuss family planning, please contact a healthcare professional

Background

Valproate treatment and reproductive risks

Valproate (as sodium valproate, valproic acid or valproate semisodium) is authorised for the treatment of epilepsy and bipolar disorder. Valproate is known to have potential risks of major congenital malformations or neurodevelopmental disorders in children when mothers take valproate during pregnancy. More recently, the risk of a range of neurodevelopmental disorders in children born to fathers taking valproate compared to other antiseizures medicines has been described.

Studies have shown that the use of valproate during pregnancy is associated with risks of physical defects, in around 1 in 9 babies exposed, and neurodevelopmental disorders, in around 3-4 in 10 babies when mothers use valproate in pregnancy. There is a much lower potential risk of neurodevelopmental disorders, in around 5 in 100 babies when fathers take valproate in the 3 months before conception. Additional reproductive risks of valproate in male patients include infertility in humans and evidence of testicular toxicity in animals.

In 2022, the Commission on Human Medicines (CHM) reviewed the latest data on the reproductive risks with valproate. Their advice was communicated in Drug Safety Update December 2022. The CHM formed an implementation group to advise on the safe introduction of the new measures into clinical practice.

The measures were applied first to all new patients under 55 years old and women of childbearing potential already under specialist review. The National Patient Safety Alert on 28 November 2023 and Drug Safety Update January 2024 provided further advice on the implementation of these requirements.

No requirement for specialist review of men currently taking valproate was introduced at this time unless the male patient was planning to father a child. The CHM recommended that any further measures should consider advice from healthcare professionals and patients developed in light of experience with the initial phase.

Recent review and updated advice

Review by two specialists remains in place for all patients initiating valproate under 55 years of age but the CHM has advised that it will not be required for men (or males) currently taking valproate. Given the recent recommendations in Drug Safety Update September 2024, the CHM advised that there is already sufficient risk minimisation in place for this patient group but that this position should be kept under review. In addition to the Drug Safety Update September 2024, further information on the reproductive risks for males can be found in a Public Assessment Report published in November 2023. Any patient wishing to change their medication should be referred to a specialist.

The information considered by CHM and the advice issued is presented in a Public Assessment Report.

Three infographics have been produced to clarify in which instances two specialist review may be required:

- for female patients under 55 years old
- for male patients under 55 years old
- for male and female patients 55 years and older

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.

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Letters and medicine recalls sent to healthcare professionals in January 2025

A summary of recent letters and notifications sent to healthcare professionals about medicines and medical devices.

Letters

In January 2025, the following letters were sent or provided to relevant healthcare professionals:

- Veoza▼ (fezolinetant): risk of drug-induced liver injury and new recommendations on monitoring of liver function before and during treatment
- Sodiofolin® (folinic acid) 50mg/ml solution for injection/infusion, strengths 100mg and 400mg, batches C240164A, C240218B and C240218C, PL 11587/0005 – requirement to use a PES or PVDF filter due to observation of particles and potential risk of thrombo-embolic event
- Dectova (zanamivir hydrate) solution for infusion 10mg/mL: Interim supply of EU shared pack stock to mitigate United Kingdom (UK) supply disruption
- Dectova (zanamivir hydrate) solution for infusion 10mg/mL: important information for healthcare professionals about the expiry date of certain batches
- Updated Imvanex suspension for injection - smallpox and mpox vaccine (live modified vaccinia virus ankara) modified vaccinia ankara - interim supply of EU stock to mitigate supply disruption
- Kineret® (anakinra) 100 mg solution for injection in a pre-filled syringe: interim supply of foreign packs to mitigate supply disruption of UK packs (PLGB 30941/0018)
- Notification of Seroxat® (paroxetine hydrochloride) 10mg, 20mg and 30mg tablets discontinuation

Medicine Recalls and Notifications

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

Class 2 Medicines Recall: Bristol Laboratories Limited, Amlodipine Bristol Lab 2.5 mg Tablets, EL (25)A/04. Issued 30 January 2025. Bristol Laboratories Limited is recalling the batches specified in this notification as a precautionary measure due to possible microbial contamination.

UPDATE: Class 2 Medicines Recall: Tesco Health Dry Cough Relief 200ml, Asda Strong Dry Tickly Cough 200ml, Almus Dry Cough Relief & Bells Dual Action Dry Cough, EL(25)A/03. Issued 22 January 2025. Bells Healthcare is recalling the listed batches of

dextromethorphan hydrobromide BP containing products as a precautionary measure, due to foreign material detected in some bottles.

Class 4 Medicines Notification: Irbesartan 150 mg and 300 mg film-coated tablets, EL(25)A/02. Issued 13 January 2025. Jubilant Pharmaceuticals NV has informed the MHRA that the Patient information leaflet (PIL) in the cartons for the batches listed in this notification include an outdated PIL.

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