Medicines & Healthcare products Regulatory Agency

DRUG SAFETY UPDATE (DSU)

Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell▼): updated safety and educational materials to support patient discussion on reproductive risks

Specialisms: *Neurology, Obstetrics, gynaecology and fertility, Psychiatry, General Practice, Pharmacy, Paediatrics and neonatology*

Summary

Updated safety and educational materials are now available to support the implementation of the regulatory measures announced in the November 2023 National Patient Safety Alert and the September 2024 Drug Safety Update. They also include previous updates to product information on the risk of low birth weight in children exposed to valproate during pregnancy.

Advice for Healthcare Professionals:

- updated safety and educational materials are now available to support healthcare professionals and patients to implement the existing regulatory requirements
- the updates reflect:
  - precautionary advice on the potential risk of neurodevelopmental disorders in children fathered by men taking valproate around the time of conception
  - a risk of lower weight at birth for the gestational age in children exposed to valproate during pregnancy
- healthcare professionals should review the new materials and integrate them into their clinical practice when referring patients and when prescribing or dispensing valproate

As a reminder

- 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

- valproate must not be prescribed to any woman or girl able to have children unless the conditions of the Pregnancy Prevention Programme (PPP) are followed
- as a precaution, recommend that male patients use effective contraception (condoms, plus contraception used by the 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. For further information see the September 2024 Drug Safety Update
- report suspected adverse reactions associated with valproate on Yellow Card

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
- women and girls who are able to have children and who are taking valproate must follow the conditions of the Pregnancy Prevention Programme
- as a precaution it is recommended that male patients taking valproate should use effective contraception (condoms, plus contraception used by the female sexual partner) throughout the valproate treatment period and for 3 months after stopping valproate
- if you are on valproate, please attend any offered appointments to discuss your treatment plan and talk to a healthcare professional if you are concerned. If you wish to discuss family planning, please contact a healthcare professional
- consult the Patient Information Leaflet and Patient Guide for men or Patient Guide for women for information about the risks of valproate – also the MHRA information page for information resources

Background

In September 2024, precautionary advice was communicated in Drug Safety Update on a potential risk of neurodevelopmental disorders in children fathered by men taking valproate around the time of conception. In February 2025, a Drug Safety Update communicated that review by two specialists remains in place for all patients initiating valproate under 55 years of age but the Commission on Human Medicines had advised that it will not be required for men (or males) currently taking valproate. Three infographics were published 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

Risk of lower weight at birth for gestational age

Product information has been updated to reflect epidemiological studies (please see references in 'Additional Information' section) which have reported a decrease in mean birth weight, and a higher risk of being born with a low birth weight (<2500 grams) or small for gestational age (defined as birth weight below the 10th percentile corrected for their gestational age, stratified by gender) for children exposed to valproate in utero in comparison to unexposed or lamotrigine-exposed children.

Updated safety and educational materials

Safety and educational materials have been updated in line with the current regulatory position and to reflect feedback from stakeholders.

The following new or updated safety and educational materials are now available online:

- Annual Risk Acknowledgement Form for female patients
- Risk Acknowledgement Form for male patients starting valproate
- Patient guide for women
- Patient guide for men
- Patient card
- Booklet for healthcare professionals
- Valproate dispensary poster

The Marketing Authorisation Holders will be sending hard copies of the materials to healthcare professionals from July 2025.

Valproate COVID-19 guidelines

The valproate COVID-19 guidance, which provided temporary advice for management of the Pregnancy Prevention Programme during the coronavirus pandemic was published in May 2020. This guidance has now been retired.

The Summary of Product Characteristics for valproate containing products outlines the conditions of the Pregnancy Prevention Programme but does not specify how a review with a patient should be held. If remote consultations are considered appropriate these should be conducted in line with relevant local clinical guidance.

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

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