NHS
North East London

January 2025 (updated)

Guidance note for the safe prescribing of valproate

Valproate (sodium valproate, valproic acid and valproate semisodium) is primarily used in epilepsy and bipolar disorder. It is also used outside of the license ('off label') to treat other conditions. Valproate is associated with a significant risk of physical birth abnormalities and developmental disorders. This guidance notes applies to prescribing clinicians in primary care. It has been developed to support the implementation of the new Medicines and Healthcare Regulatory Agency (MHRA) regulatory measures for oversight of prescribing to new patients and existing girls and women of childbearing potential prescribed valproate and precautionary safety measures for valproate use in boys and men of reproductive potential. New evidence has shown a possible association between valproate use in men at conception with increased risk of neurodevelopmental disorders in children. The updated safety measures are summarised below:

All patients aged under 55 years	
All initiations in new patients under 55 years must be agreed by two independent specialists with documented evidence that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.	
Men and boys of reproductive potential	**Women and girls of childbearing potential**
Risk of infertility and neurodevelopmental disorders in children when taken at conception.	Risk of physical birth abnormality and neurodevelopmental disorders in children when exposed during pregnancy.
Precautionary advice to not donate sperm during treatment with valproate and for three months after stopping valproate.	Must not be used unless the conditions of the Pregnancy Prevention Programme (PPP), PREVENT are met.
Two specialists must complete and sign the Risk Acknowledgment Form (RAF) for patients under the age of 55 years that are newly initiated on valproate (however the RAF does not need to be completed for patients that are currently on valproate)	Two specialists must sign the form for new patients initiating valproate under 55 years of age and thereafter annual review and Annual Risk Acknowledgement Form (ARAF) completion with a single signature is required.
No mandatory annual specialist review but discussions about reproductive risks should take place as part of usual care.	Annual specialist review required for all female patients on valproate to reassess treatment need and risks.

Actions for primary care prescribing clinicians

- Initiate an EMIS (or SystmOne) search to identify patients prescribed valproate.
- Check that all girls and women of childbearing potential under 55 years prescribed valproate have a valid Annual Risk Acknowledgement Form (ARAF).
- Check that all newly initiated male patients under 55 years of age prescribed valproate have a valid Risk Acknowledgment Form (RAF).
- Advise patients not to stop taking valproate unless they are advised to do so by a healthcare professional.
- Ensure all patients are aware of the reproductive risks (e.g. infertility) and risk of foetal harms when unborn children are exposed to valproate during pregnancy and at conception.

- Please discuss the pregnancy prevention programme with all patients of childbearing potential and record the outcome using the using the Clinical Excellence Group (CEG) **'Valproate Monitoring NEL Template'**.
- Ensure the ARAF and RAF are coded on EMIS (or SystmOne) using the CEG '**Valproate Monitoring NEL Template'**.
- Please discuss contraceptive methods with all patients prescribed valproate. Refer to the Healthcare Professional Guide for further information on the risk of valproate use in patients.
- In women and girls of childbearing potential prescribed valproate, highly effective methods (typical-use failure rates of less than 1%) e.g. sterilisation and long-acting reversible contraceptive (LARC) methods (intrauterine devices and implants) are preferred. Alternatively, two complementary contraceptive methods and it must include a barrier method**.** Follow the advice from the MHRA on contraceptive methods for women taking medicines with teratogenic potential.
- If a female patient reports they are pregnant or planning a pregnancy with a man on valproate (including those undergoing IVF), refer for prenatal counselling
- In boys and men of reproductive potential, as a precaution recommend that 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. Follow the advice for male patients on valproate to use contraception and consult the visual risk communication diagram when counselling on the risks.
- At the next regular treatment review, discuss with men and boys of reproductive potential on oral valproate treatment whether they are planning a family in the next year and if they are, refer to a specialist to discuss alternative treatment options. There is a potential small increased risk of the child being diagnosed with a mental or movement related developmental disorder (neurodevelopmental disorder).
- Advise men not to donate sperm during valproate treatment and for 3 months after stopping valproate.
- Prescribe appropriate quantities so that pharmacists can dispense a manufacturer's original full pack which will include all the necessary safety information for the patient.
- Where it is not in a patient's best interests to prescribe a full original pack, please document the reason in the patient record.
- Ensure all patients of childbearing potential have an annual specialist review.
- For further information please consult the MHRA guidance on valproate use by women and girls and drug safety update on valproate use in men.

Patient Information

Patient guide to be provided to all girls and women of childbearing potential (or those responsible for their care) who are started on, or continue to use, valproate.
Patient card to be given by pharmacists to all female patients (or those responsible for their care) who are dispensed valproate to inform them of the risks.
Decision tool**:** Support tool for women and girls of childbearing potential with epilepsy to guide decisions about taking valproate.
Decision tool: Support tool for women and girls of childbearing potential with bipolar to guide decisions about taking valproate.

Patients may wish to talk to an epilepsy or mental health charity:

- Bipolar UK: 0333 323 3880
- Epilepsy Action: 0808 800 5050
- Epilepsy Society: 01494 601 400
- Mind: 0300 123 1234
- Young Epilepsy 01342 831342

Please continue to record suspected adverse drug reactions to the Yellow Card scheme.
Please continue to record medicine patient safety incidents to Learning From Patient Safety Events

References

1. MHRA regulatory measures for oversight of prescribing to new patients and existing girls and women of childbearing potential prescribed valproate
2. MHRA guidance on valproate use by women and girls
3. MHRA drug safety update on valproate use in men.

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