



## **VALPROATE: safe prescribing and dispensing to girls of any age and women of childbearing potential**

- **Licensed use of valproate medicines in girls and women of childbearing potential requires a Pregnancy Prevention Programme to be in place.**
- **Valproate treatment must be started and supervised by an experienced specialist.**
- **Fulfilment of the conditions of the Pregnancy Prevention Programme must be checked at each point of prescribing and dispensing.**

Valproate (Epilim, Depakote, Convulex, Episenta, Epival, Kentlim, Orlept, Sodium Valproate, Syonell, Valpal) contains valproic acid, an active ingredient with known teratogenic effects. 10.73% of children of women who have epilepsy exposed to valproate during pregnancy suffer congenital malformations. 30–40% of children with a history of valproate exposure in utero experience delays in their early development.

The conditions of the valproate Pregnancy Prevention Programme (**prevent**) also concern girls of any age and women who are not currently sexually active unless the specialist considers that there are compelling reasons to indicate that there is no risk of pregnancy. Individual circumstances should be evaluated in each case, involving the patient or carer, or both in the discussion, to guarantee engagement, discuss therapeutic options and ensure understanding of the risks and the measures needed to minimise the risks.

### **Specialist prescribers**

- Do not consider treatment with valproate in female patients of childbearing potential unless other treatments are ineffective or not tolerated.
- Review girls and women who may be of childbearing potential at least annually.
- Every effort should be made to switch female children to alternative treatment before they reach adulthood [1].
- See the patient urgently (within days) if referred back in case of unplanned pregnancy or if she wants to plan a pregnancy.

### *When considering treating girls and women of childbearing potential*

- Provide a Patient Guide and discuss the risks with the patient or carer, or both.

### *Before prescribing valproate*

- Exclude pregnancy by performing a serum pregnancy test.
- Arrange for highly effective contraception\*.

### *If it is necessary to treat or continue to treat girls or women of childbearing potential*

- Discuss the need for her to be on the prevent programme.
- Complete the Annual Risk Acknowledgment Form with patient or carer, or both; give them a copy and send a copy to the GP.

\* At least one highly effective method of contraception (preferably a user independent form such as an intrauterine device or implant) or two complementary forms of contraception including a barrier method should be used.

**General practitioners**

- Refer new presentations of epilepsy or mental health disorders to the relevant specialist for diagnosis, to initiate treatment, and assess the need for highly effective contraception.
- Refer existing patients back to the specialist for annual review if they have been discharged from the service.
- Arrange to see each patient after specialist review and check the conditions of the valproate Pregnancy Prevention Programme have been fulfilled.
- Check for the continuous use of **highly effective contraception**<sup>†</sup> in girls and women of childbearing potential.
- Consider the need for urine pregnancy testing for girls from 12 years of age [2] based on the failure rate of the type(s) of contraception used and the information provided by the patient.
- If there is a risk of pregnancy a urine pregnancy test should be completed. However, it may not be necessary to complete a pregnancy test at each follow up appointment.
- Refer a patient planning to become pregnant to her specialist. Inform her not to stop contraception or valproate until told to by her specialist.
- Refer a patient with unplanned pregnancy to her specialist and ask for her to be seen urgently (within days). Inform her not to stop valproate.
- **Check that all patients have an up to date, signed, Annual Acknowledgment of Risk Form each time a repeat prescription is issued.** Ongoing supply without an up to date, signed, Annual Acknowledgment of Risk Form should be based on an assessment of the patient's needs.
- Tell her to contact you immediately if she suspects there has been a problem with her contraception or she may be pregnant.

**Off-label use**

In circumstances where the conditions of the valproate Pregnancy Prevention Programme cannot be met it may be in the patient's best interest for prescribing to continue. Such off-label use requires the prescriber to, "take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring and follow-up" [3]. Specialists must support generalists and meet as fully as possible the conditions of the Pregnancy Prevention Programme following best practice for communication and record keeping [4]. If it is necessary to continue, the rationale should be clearly documented.

**Pharmacists**

- Ensure the Patient Card is provided every time valproate is dispensed. If it is confirmed that the patient already has a card, clearly document in the clinical record if no card is supplied.
- Remind patients of the risks in pregnancy and the need for highly effective contraception<sup>†</sup>
- Remind patients of the need for annual specialist review.
- Ensure the patient has received the Patient Guide.
- Dispense valproate in the original package. In situations where repackaging cannot be avoided, always provide a copy of the package leaflet and add a sticker with the warning to the outer box.
- If a woman of childbearing potential reports that she is not taking highly effective contraception<sup>†</sup>, refer them to their GP (including by contacting the GP if necessary).

**Gynaecologists/obstetricians, midwives and nurses**

- Provide counselling on contraception methods and pregnancy planning.
- Provide information about the risks of using valproate during pregnancy.
- When a patient consults for pregnancy refer her and her partner to her prescriber and to a specialist experienced in prenatal medicine for evaluation and counselling regarding the exposed pregnancy.

**Emergency physicians**

- Ensure that any woman of childbearing potential using valproate is referred to her specialist for assessment.
- If she is pregnant, ensure that she is referred for urgent review (within days).

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<sup>†</sup> At least one highly effective method of contraception (preferably a user independent form such as an intrauterine device or implant) or two complementary forms of contraception including a barrier method should be used.

## Resources

### Medicines and Healthcare Products Regulatory Agency (2019)

*Valproate use by women and girls*. [online] Available at <https://www.gov.uk/guidance/valproate-use-by-women-and-girls> [Accessed 08 January 2019]

[Patient card](#)   [Patient booklet](#)

[Booklet for healthcare professionals](#)

[Valproate annual risk acknowledgement form](#)

### Royal College of General Practitioners, Association of British Neurologists and Royal College of Physicians (2019)

*Valproate Use In Women and Girls Of Childbearing Years*. [online] Available at <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/valproate-use/> [Accessed May 2019]

### Medicines for Children

*Sodium valproate for preventing seizures*. [online] Available at <https://www.medicinesforchildren.org.uk/sodium-valproate-preventing-seizures> [Accessed 23 Nov 2018]

*Sodium valproate and pregnancy - information for parents and carers*. [online] Available at <https://www.medicinesforchildren.org.uk/sodium-valproate-and-pregnancy-information-parents-and-carers> [Accessed 23 Nov 2018]

*Sodium valproate and pregnancy - information for girls and young women*. [online] Available at <https://www.medicinesforchildren.org.uk/sodium-valproate-and-pregnancy-information-girls-and-young-women> [Accessed 23 Nov 2018]

## References

1. Medicines.org.uk (2018). *Epilim 200 Gastro-resistant tablets – Summary of Product Characteristics (SPC) – (eMC)*. [online] Available at <https://www.medicines.org.uk/emc/product/519> [Accessed 16 October 2018]
2. Royal College of Paediatrics and Child Health. Pre-procedure pregnancy checking for under-16s: clinical guideline. [online] Available at <https://www.rcpch.ac.uk/resources/pre-procedure-pregnancy-checking-under-16s-clinical-guideline> Accessed [16 October 2018]
3. Medicines and Healthcare Products Regulatory Agency (2018). *Off-label or unlicensed use of medicines: prescribers' responsibilities*. [online] Available at <https://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities> [Accessed 16 October 2018]
4. General Medical Council (2013). *Good medical practice*. [online] Available at <https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices> [Accessed 16 October 2018]