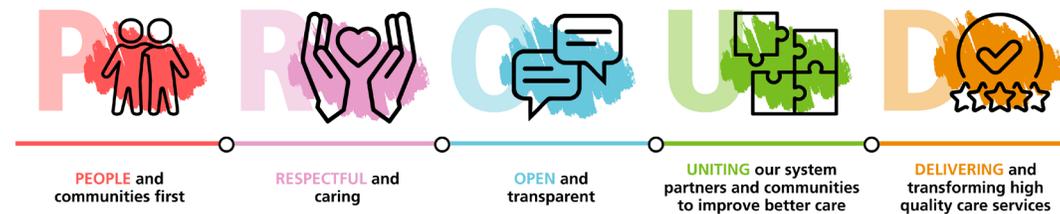


Valproate

Lancashire and South Cumbria Medicines Optimisation Team



Agenda

Agenda	Time	Speaker
Valproate background and new regulations	20 minutes	Tara Gallagher
Local pathways and monitoring	10 minutes	Nicola Baxter and MO team
Q&A and close	10 minutes	

Objectives

- Understand the current risks and measures to mitigate risks associated with valproate use in women of childbearing potential and men of reproductive potential.
- To share resources, local pathways and monitoring of the Medicines Optimisation LES.

Background

Valproate and risk of congenital defects and neurodevelopmental disorders

- Valproate use in females:
 - Valproate can cause birth defects in 1 in 9 (11%) children
 - 3 or 4 in every 10 will have serious development problems e.g. autism, learning disability, and possibly ADHD
- Valproate use in males:
 - Potential increased risk of neurodevelopmental conditions in a child conceived by a male taking valproate
 - In addition, potential risk of infertility and testicular toxicity

Lifetime cost of one baby born with each condition

Learning and development problems

Autism £2,409,000
ADHD £124,000
Speech, language and communication needs £90,000
Dyslexia £50,000
Dyspraxia £75,000

Physical disabilities

Spina bifida £927,000
Facial and skull malformations £11,000

Low birth weight

No reliable estimate found



These costs are incurred by the affected families, the NHS, the education system, the welfare system, and wider society

Background

- November 2023: National Patient Safety Alert (NatPSA) on valproate: organisations to prepare for new regulatory measures for oversight of prescribing to new patients and existing female patients
- September 2024: MHRA Update: valproate use in men: as a precaution, men and their partners should use effective contraception
- February 2025: MHRA Update: review by two specialists is still required for all initiating valproate, once for all women already taking but not for male patients already taking valproate. Three infographics published to clarify in which situations a review by two specialists may be required

Background

- June 2025: MHRA Update:
- 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

Valproate – New Regulations

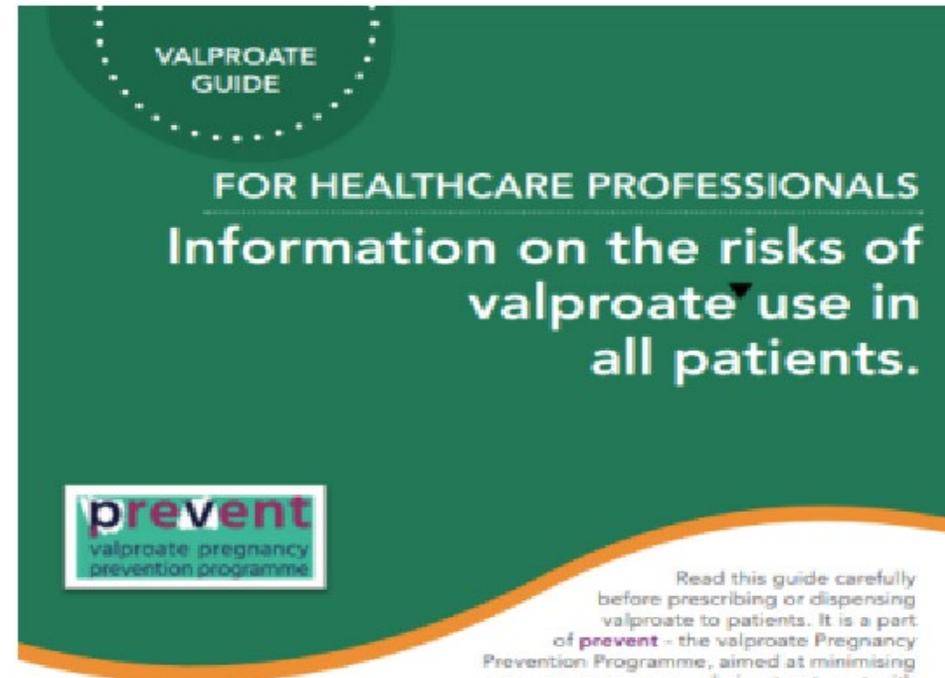
- **NEW STARTERS** - Valproate must not be started in new patients (male or female) younger than 55 years unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.
- **WOMEN ALREADY ON VALPROATE** - at their next annual specialist review, women of childbearing potential and girls receiving valproate should be reviewed using the revised valproate Annual Risk Acknowledgement Form. A second specialist signature will be needed if the patient is to continue on valproate, however subsequent annual reviews will only require one specialist unless the patient's situation changes.
- Revised Annual Risk Acknowledgement Form for females (ARAF).
- New Male Risk Acknowledgement Form (RAF) for new initiations of valproate in males.
- General practice - should continue to prescribe valproate and if required offer patients a referral to a specialist to discuss their treatment options.

Updated safety and educational materials: June 2025

- 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 sent hard copies of the materials to healthcare professionals from July 2025.

Healthcare professionals Guide



Read this guide carefully before prescribing or dispensing valproate to patients. It is a part of **prevent** - the valproate Pregnancy Prevention Programme, aimed at minimising pregnancy exposure during treatment with valproate. (This programme will be referred to as **prevent** throughout this guide). It also includes information on the risks of valproate for male patients.

It is recommended that pregnant women taking antiepileptic drugs in general, and valproate in particular are enrolled in the UK Epilepsy and Pregnancy Register (<http://www.epilepsyandpregnancy.co.uk>). This should be done as early as possible in the patient's pregnancy.

This medicine will be referred to as valproate throughout this guide and covers the brands Epilim, Depakote, Convulex, Episenta, Epival, Sodium Valproate, Syonell, Belvo & Dyzantil.

Patient Card

Valproate ▼ (Epilim, Depakote, Convulex, Episenta, Epival, Sodium Valproate, Syonell, Belvo & Dyzantil): Contraception and Pregnancy Prevention

What you must do

- Do not stop taking valproate unless your specialist tells you to as your condition may become worse.
- If you are thinking about having a baby, do not stop taking valproate or using birth control (contraception) before speaking to your specialist.
- If you think you are pregnant, do not stop taking valproate unless your specialist tells you to. Make an urgent appointment with your general practitioner to be urgently referred to your specialist.
- Read the package leaflet carefully before use.
- Read the Patient Guide for **prevent** – the valproate Pregnancy Prevention Programme. You should have received a copy from your specialist, or it can be accessed online using the QR code on the leaflet in the pack.



MAT-XU-2305387 (v2.0)

May 2025

All girls and women using valproate and who could become pregnant:

- Valproate is an effective medicine for epilepsy and bipolar disorder.
- Valproate can seriously harm an unborn baby when taken during pregnancy and may lead to permanent disability.
- Use an effective method of birth control (contraception) at all times during your treatment with valproate.
- It is important to discuss and review your treatment with a specialist at least once each year.

Males using valproate:

- There is a possible risk of neurodevelopmental conditions in children when valproate is taken by the father in the 3 months before conception.
- Discuss this possible risk and the need for yourself and your female partner to use effective contraception with your doctor.

▼ These medicines are subject to additional monitoring. Report any side effects to www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Keep this card safe so you always know what to do.

Patient guide for women

THIS GUIDE IS FOR FEMALE PATIENTS TREATED WITH VALPROATE WHO CAN BECOME PREGNANT

PATIENT GUIDE:
What you need to know about valproate

prevent

Read this guide along with the patient information leaflet which is included in each box of your medicine

This medicine will be referred to as valproate throughout this guide and covers the brands Epilin, Depakote, Convulex, Episenta, Eptival, Sodium Valproate, Syonell, Balvo & Dyzantil.

This guide contains key information about the risk of valproate use during pregnancy.

KEEP THIS GUIDE. YOU MAY NEED TO READ IT AGAIN.

Information about the use of valproate in female patients who can become pregnant and risks of valproate use during pregnancy can also be found online at www.medicines.org.uk by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines listed. You can also search online for "MHRA valproate".



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Patient guide for men

VALPROATE GUIDE FOR MALE PATIENTS

Read this guide along with the patient information leaflet which is included in each box of your medicine

This medicine will be referred to as valproate throughout this guide and covers the brands Epilin, Depakote, Convulex, Episenta, Eptival, Sodium Valproate, Syonell, Balvo & Dyzantil.

WHAT YOU SHOULD KNOW

This guide contains key information about the risks of valproate. Ask your doctor, nurse or pharmacist if you have any questions.

KEEP THIS GUIDE. YOU MAY NEED TO READ IT AGAIN.

Information about the use of valproate in male patients can also be found online at www.medicines.org.uk by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines listed. You can also search online for "MHRA valproate".



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Risk acknowledgement form for female patients

Updated June 2025

There are four steps to the form:

- Step 1 – Specialist prescriber:

Establish whether the patient is at risk of the reproductive harms of valproate

- Step 2: Specialist prescriber and countersigning specialist: Document the prescribing decision.
- Step 3: Specialist prescriber: Explain the risks to the patient or responsible person.
- Step 4: To be completed by the patient or responsible person.

Annual Risk Acknowledgement Form for Female Patients VALPROATE HAS RISKS IN PREGNANCY

Children exposed to valproate during pregnancy have a high risk for congenital malformations, neurodevelopmental disorders and lower weight at birth for gestational age.

Valproate should not be used in female patients aged under 55 years unless two specialists (specialist prescriber and countersigning specialist) independently consider and document, in this form, that there is no other effective or tolerated treatment. This form outlines the conditions of **prevent** - the valproate Pregnancy Prevention Programme and when these must be fulfilled.

Female patients who have a permanent reason that they do not have the potential to get pregnant (e.g., post-menopausal patients or those after hysterectomy) do not need to complete this form beyond step 1. This form can be used to support documentation in the medical notes that **prevent** does not apply to this patient.

- This form is used to support and record the prescribing decision and, where applicable, discussion with the patient or their responsible person of the risks associated with the use of valproate during pregnancy and the measures needed to minimise the risks in female patients.
- The specialist prescriber must provide this form to female patients treated with valproate (Epilem, Depakote, Convulex, Episoeta, Epival, Sodium Valproate, Synovel, Belvo & Dyanell) - or to their "responsible person" i.e., a parent/legal guardian or person capable of giving consent on behalf of patients who are minors or without the capacity to make an informed decision, or a person acknowledging that the treatment is in the best interests of the patient.
- The decision of the countersigning specialist must be documented in step 2. A countersigning specialist is only required for patients newly starting valproate and for existing female patients at one annual review. Subsequent annual reviews do not require the countersigning specialist unless the patient's circumstances have changed. The date of the second specialist review should be included in this and all subsequent ARAFs.
- This document can be completed electronically, wet signatures are not required.

Once completed, a copy of this form should be given to the patient or their responsible person and stored in their medical notes, it should also be shared with all healthcare professionals listed in the table below.

Name of patient:	Patient's date of birth:
Patient's NHS number:	Patient's hospital number:
Name and contact details of specialist prescriber:	Role and unique identifier:
Signature of specialist prescriber:	Date of signature:

Name of countersigning specialist:	Role and unique identifier:
Signature of countersigning specialist (if needed specialist prescriber can sign here to confirm that discussion with countersigning specialist has occurred):	Date of signature: This date should be included in step 2 within this ARAF and all subsequent ARAFs.

Name and address of patient's General Practitioner (GP):

Date form completed:

WARNING: Prescribing valproate to a woman of childbearing potential without the conditions of **prevent** - the Pregnancy Prevention Programme being fulfilled is contraindicated and represents an unlicensed use of the drug. Use of valproate during pregnancy for bipolar disorder, and during pregnancy for epilepsy (unless there is no other effective or tolerated treatment), are both unlicensed. This is the case even when treatment is based on an informed choice made by the patient.

More information can also be found online at www.medicines.org.uk by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines listed.

MAT-XU-2305459 (v2.0)

May 2025

Exceptions to PREVENT

- FEMALES - If there is a compelling reason pregnancy will not take place
 - Postmenopausal
 - Hysterectomy
 - Severe intellectual disability
- MALES - If there is a compelling reason the risks do not apply
 - Vasectomy
 - Other reason for infertility
 - Severe intellectual disability

Valproate – Treatment in males

- Valproate may cause infertility, likely reversible if valproate is stopped or dose reduced
- Possible testicular toxicity
- A post-authorization safety study (PASS) to evaluate the paternal exposure to valproate and the risk of neurodevelopmental disorders (NDD) and congenital abnormalities in offspring in Nordic countries
- Comparing risk of NDD in offspring to men taking valproate vs lamotrigine/levetiracetam 3 months before conception.
- 5% risk of NDD if the man took Valproate vs 3% if the man took lamotrigine/levetiracetam

<https://www.gov.uk/government/news/mhra-update-on-new-study-on-risk-in-children-born-to-men-taking-valproate>

Advice for male patients on valproate

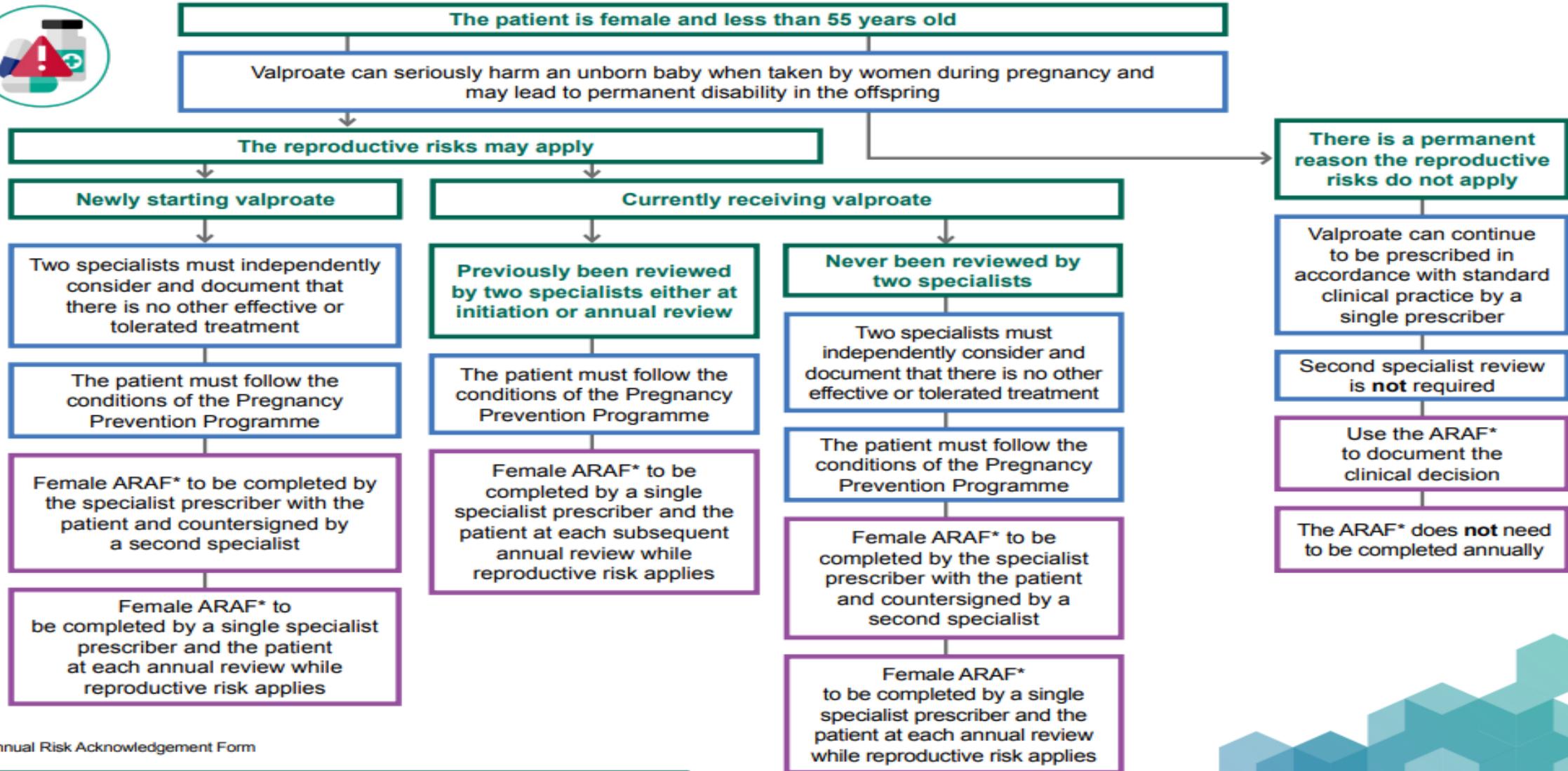
- Male patients (of any age) – if they father a child while taking valproate or in the three months after stopping valproate, there is a potential small increased risk of the child being diagnosed with a mental or movement related developmental disorder (neurodevelopmental disorder). Inform male patients (of any age) who may father children of the possible risk at initiation of valproate or at their next regular treatment review.
- Inform male patients (of any age) who may father children of the possible risk at initiation of valproate or at their next regular treatment review – this counselling should be given irrespective of the indication for valproate and also after intravenous use of valproate
- 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

Advice for Males on valproate

- At the next regular treatment review, discuss with men 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
- 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
- Advise men not to donate sperm during valproate treatment and for 3 months after stopping valproate
- Report any suspected adverse drug reactions associated with valproate on a [Yellow Card](#)
- Full Guidance:
- <https://www.gov.uk/drug-safety-update/valproate-use-in-men-as-a-precaution-men-and-their-partners-should-use-effective-contraception>

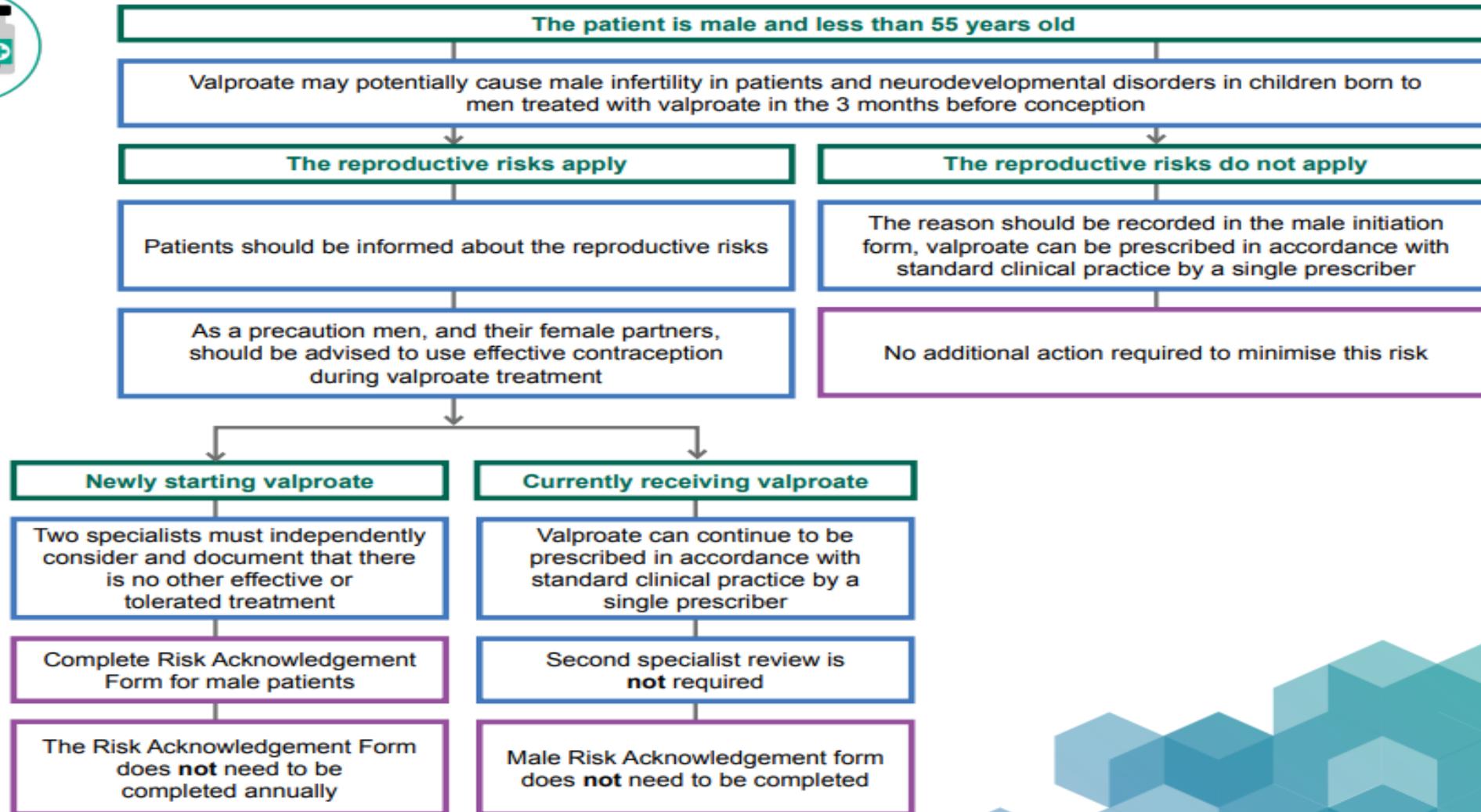
February 2025 MHRA update and infographics

- February 2025: MHRA Update: review by two specialists is required for initiating valproate but not for male patients already taking valproate
- Three infographics published in which situation review by two specialist may be required:
 - Female patients under the age of 55 years old
 - Male patients under the age of 55 years old
 - Female and male patients over the age of 55 years



*Annual Risk Acknowledgement Form

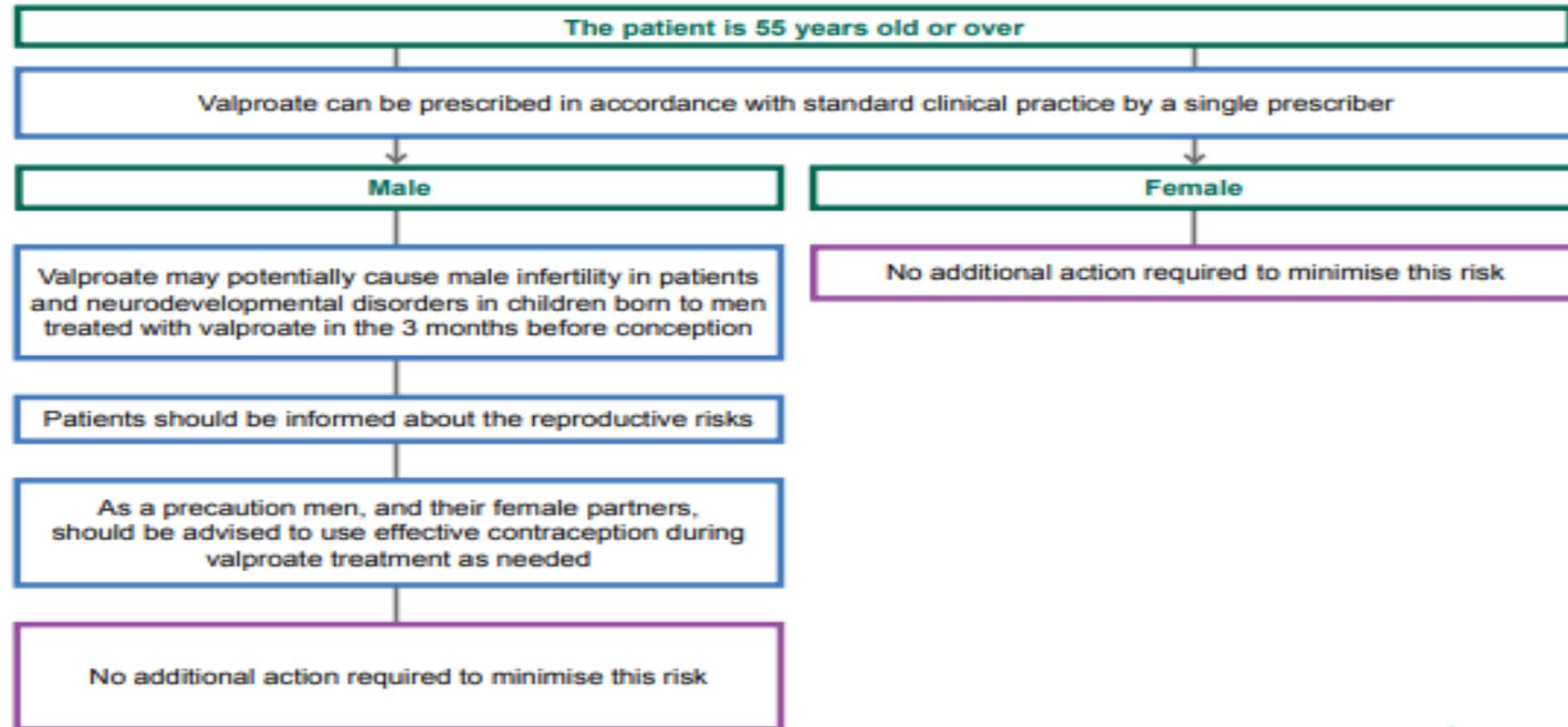
Key: — Decision point — Advice — Risk minimisation activity



Key: — Decision point — Advice — Risk minimisation activity



Risk minimisation measures required for Valproate prescribing



Key: — Decision point — Advice — Risk minimisation activity

Valproate - decision support tool

Is valproate the right epilepsy treatment for me?



Valproate is also known as: Sodium valproate, Valproic acid, Epilin, Episenta, Epival, Convulex, Syonell, Belvo, Orlept, Depakote, Dyzar

I'm taking valproate

Page 2 of 6

This information is for women, girls and anyone who is pregnant, aged under 55, taking valproate for epilepsy

Valproate is also known as: Sodium valproate, Valproic acid, Epilin, Epilin Chrono, Epilin Chronosphere, Episenta, Epival, Convulex, Syonell, Belvo, Orlept, Depakote, Dyzantil, Depakin

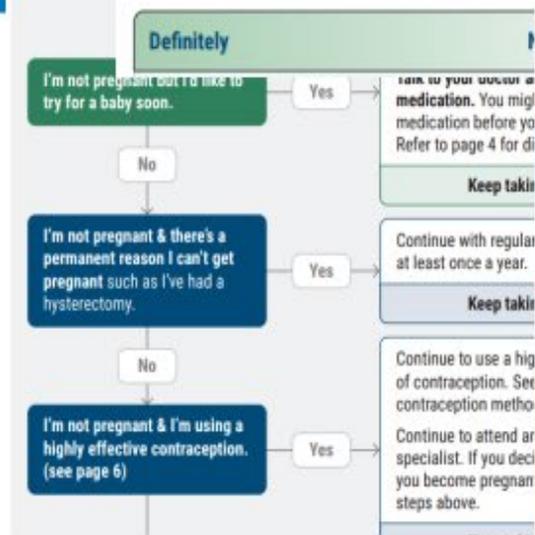
This information is important because you may become pregnant if you are taking valproate.

This is because if you take valproate while pregnant it can harm your baby and cause learning difficulties.

What's important to you?

Page 3 of 6

Your personal feelings are an important part of making a decision. Think about what matters most to you in this decision.



Potential benefits and harms to my baby

Page 4 of 6

You continue to take valproate

(Sodium valproate, Valproic acid, Epilin, Epilin Chrono, Epilin Chronosphere, Episenta, Epival, Convulex, Syonell, Belvo, Orlept, Depakote, Dyzantil, Depakin)

You change medication

(Carbamazepine, phenobarbital, phenytoin, lamotrigine (Lamictal), levetiracetam (Keppra), topiramate, pregabalin)

Benefits to you

- Your seizure control remains the same
- If you are able to drive, this will continue
- Your normal lifestyle can continue
- Valproate may be the best drug to control your type of epilepsy

- You may lose weight
- You may be less sedated
- If you have a tremor it may resolve
- Your periods might become more regular

How effective is your contraception?

Page 5 of 6

No contraception is 100% effective.

Highly effective means a risk of less than 1 out of every 100 women would get pregnant in a year. Talk to your doctor or healthcare provider about choosing a suitable contraception for you.

How many women, out of every 100, would get pregnant in one year if they used in a typical way:

MHRA Aide Memoir Table



Medicines & Healthcare products
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Pregnancy testing and contraception for pregnancy prevention during treatment with medicines of teratogenic potential

- **Risk of pregnancy should be assessed prior to each teratogen prescription**
 - Risk of pregnancy may be high at start of a method or when switching between methods due to risk of pregnancy from unprotected sex prior to starting the method, unreliable use of the previous contraceptive method, and/or time needed to establish contraceptive efficacy at the start of the new method.
 - Pregnancy tests at start of contraceptive method may not detect an early pregnancy following unprotected sex in the last 3 weeks
- **Any starter on new method contraception should have a repeat pregnancy test at 3 weeks if there is any risk of pregnancy at start of contraceptive method**
- The duration of teratogen prescriptions may need to be shortened for patients who use contraceptive methods that require frequent pregnancy testing

Effectiveness of contraceptive in typical use ¹	Contraceptive method	Duration contraceptive method used / other situations	Pregnancy test needed before next teratogen prescription?
Highly effective methods (Typical use failure rates less than 1%)	Copper intrauterine device (copper IUD)	Established user more than 3 weeks to 5 to 10 years (depending on IUD ²)	No
	Levonorgestrel-releasing intrauterine system (LNG-IUS)	Established user more than 3 weeks to 3 to 8 years (depending on IUS ²)	No
	Progestogen Implant	Established user more than 3 weeks to 3 years Established user (more than 3 weeks), but concurrent use of interacting medicines which may affect efficacy ³	No Yes + review / refer for contraceptive advice
Effective methods (Typical use failure rates greater than 1%)	Depot medroxyprogesterone acetate (DMPA) subcutaneous (SC) or intramuscular (IM) injections ⁴	Established user (more than 3 weeks + repeat injections on schedule) and less than 13 weeks since last injection + documented as administered by healthcare professionals	No
		Established user (more than 3 weeks + repeat injections on schedule and less than 13 weeks since last injection) but self-administered or undocumented administration More than 13 weeks since last injection (ie, beyond recommended duration of use of last injection)	Yes, test if any suspected risk of pregnancy Yes + review / refer for contraceptive advice
Additional barrier methods are advised during teratogen use	Combined hormonal contraceptives (pills, patches or vaginal ring) or progestogen-only pills	Established user (more than 3 weeks), reliable and consistent use	Yes, test if any suspected risk of pregnancy
		Established user (more than 3 weeks) but with unreliable or inconsistent use of method, eg, <ul style="list-style-type: none"> • missed pills, late patch • diarrhoea or vomiting • use of other interacting medicines that may affect efficacy³ 	Yes + review / refer for contraceptive advice
Other methods or no contraception		Any duration of use of other methods	Yes + review / refer for contraceptive advice;
		No contraception	Assess need for contraception + test if any suspected risk of pregnancy + review / refer for contraceptive advice

Explanatory notes:

1. Effectiveness of methods are based on failure rates in typical use (which includes risk of user error) rather than perfect use. Perfect use failure rates are similar for specific methods listed (0.03–0.6%) but risk of user error is higher for daily methods than for long-acting reversible contraceptive (LARC) methods and are highest for methods used at time of sexual intercourse. Highly effective methods are based on less than 1% failure rate in typical use; Less effective methods are based on greater than 1% failure rate (6–9%) in typical use (Trussell J. *Contraception*, 2011; 83: pages 397 to 404).
2. Refer to Product Information for specific products; patients should be reviewed / referred for contraception advice at the end of the

BwD audit

- Initial data extraction identified 76 females in BwD prescribed valproate-containing medicines.
- Of these, 12 patients were coded as having a mental health condition or a learning disability, with an initial compliance rate of 33.3% with the PPP.
- Following a data cleansing exercise and individual follow-up, the cohort was revised to 14 patients, as two additional individuals were identified without a coded diagnosis in the original extraction.
- This follow-up revealed an improved compliance rate of 64%.

Local Resources

[Clinical areas](#)
[Non-medical prescribing](#)
[Medicines sustainability](#)
[Care homes and domiciliary care](#)
[Education and training](#)
[Useful links](#)

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LES Resources 2025 2026

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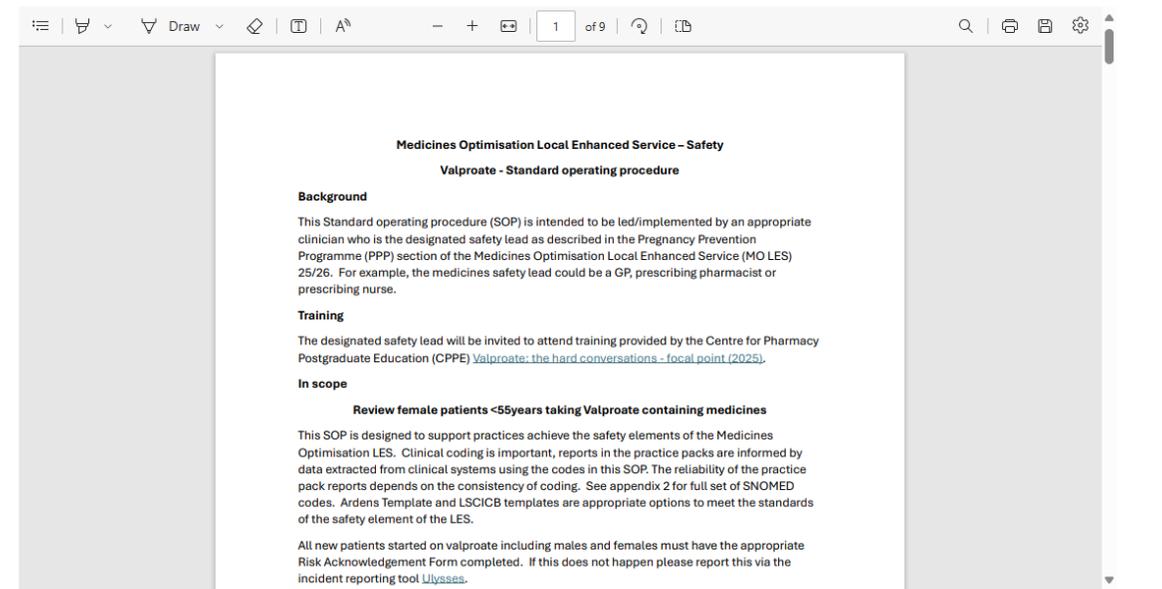
Dan Clough • Updated on 1 October 2025 11:08 am

Medicines Optimisation Service Specification	+
Resources	-
Antimicrobial Stewardship	+
Cardiovascular	+
Diabetes	+
Eclipse	+
Medicines of dependence	+
PREVENT programme	+
Repeat prescribing	+
Respiratory	+
SMRs	+
Resources for Medicine Co-ordinators/ Medicines Managers or equivalent	+
Optimise Rx	+

Valproate SOP

- Eclipse +
- Medicines of dependence +
- PREVENT programme -
- The Valproate SOP -

The Valproate SOP has been designed with primary care clinical colleagues to support practices achieve the safety elements of the Medicines Optimisation LES. Clinical coding is important, reports in the practice packs are informed by data extracted from clinical systems using the codes in this SOP.



Summary of Key Messages

- Valproate medicines must not be used in women of childbearing potential unless the Pregnancy Prevention Programme is in place.
- If you are involved in the care of female or male patients on valproate in the UK, see a reminder of actions required for this medicine.
- Valproate must not be started in new patients (male or female) under the age of 55 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
- At their next annual specialist review, women of childbearing potential and girls should be reviewed using a revised valproate Risk Acknowledgment Form (ARAF), which will include the need for a second specialist signature if the patient is to continue with valproate and subsequent annual reviews with one specialist unless the patient's situation changes.
- 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. There is a potential small increased risk of the child being diagnosed with a mental or movement related developmental disorder (neurodevelopmental disorder). Male Risk Acknowledgement Form (RAF) required for new initiations of valproate in males.





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South Cumbria**
Integrated Care Board

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