South East London Integrated Care System

NHS South East London

Primary Care Guidance for managing Medicines with Teratogenic Potential that require Pregnancy Prevention Programme

Contents

1. Background

Medicines with teratogenic potential are known or suspected to increase the risk of birth defects and developmental disorders. A drug is a teratogen if its administration to the pregnant mother, directly or indirectly, causes a structural or functional change in the foetus or child.

The Medicines and Healthcare products Regulatory Agency (MHRA) reviews evidence and publishes updates to healthcare professionals, including guidance on contraception, contraceptive methods and frequency of pregnancy testing to reduce inadvertent exposures during pregnancy in a patient taking a medicine of teratogenic potential. Additional guidance is available for medicines for which a formal Pregnancy Prevention Programme (PPP) is required.

Refer to the MHRA guidance (published 21 March 2019):
Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed?

2. Pregnancy Prevention Programme (PPP)

Pregnancy Prevention Programme (PPP) is a risk management strategy for medicines that can cause severe harm to an unborn child, ensuring that individuals of childbearing potential are not exposed to these drugs during pregnancy. This is achieved through a combination of patient education on reproductive risks, mandatory annual specialist reviews, strict adherence to effective contraception, and the annual signing of a Risk Acknowledgement Form

An individual of childbearing potential refers to a person who has a uterus and ovaries, who is pre-menopausal (from the onset of menstruation to menopause), and who can become pregnant. The requirement of PPP applies to highly teratogenic drugs, such as thalidomide, lenalidomide, isotretinoin, valproate (including sodium valproate and valproic acid), and topiramate.

Refer to the Summary of Product Characteristics (SmPC)
for specific PPP requirements and educational risk minimisation materials to help reduce the risk associated with using the medicine.

3. Contraception and Pregnancy Testing

Contraceptive methods are classified as **effective** or **highly effective** based on their typical-use failure rates in the first year

Refer to MHRA guidance: *Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed?*

When using medicines with teratogenic potential, patients should be informed of the risks and advised to use the most effective contraceptive method suited to their circumstances.

Refer to the Clinical Knowledge Summaries (CKS) guidance on Contraceptive assessment:
Scenario: Comorbidities and personal characteristics (last revised Jan 2024), which includes details on methods of contraception suitable for women taking known teratogenic drugs or drugs with potential teratogenic effects (such as lithium and sodium valproate.

The College of Sexual and Reproductive Healthcare Clinical Effectiveness Unit (CoSRH CEU) published a statement on contraception for women using known teratogenic drugs or drugs with potential teratogenic effects to support clinicians in providing high quality and consistent contraceptive advice.

CoSRH CEU recommendations:

- Women should be made aware that no method of contraception is 100% effective.
- Methods of contraception which are considered 'highly effective' in this context include the long-acting reversible contraceptives (LARC) copper intrauterine device (Cu-IUD), levonorgestrel intrauterine system (LNG-IUS) and progestogen-only implant (IMP) and male and female sterilisation, all of which have a failure rate of less than 1% with typical use. **(Note that women using IMP must not take any interacting drugs that could reduce contraceptive effectiveness).**
- Additional contraceptive precautions (e.g. condoms or a second effective contraceptive method) are not required if a Cu-IUD, LNG-IUS, IMP or male or female sterilisation is being used. However, a woman may choose to use condoms in addition to reduce risk of unintended pregnancy even further and for protection against sexually transmitted infections.
- The typical use failure rate of combined hormonal contraception (CHC) and the progestogen-only pill (POP) is 9%; for progestogen-only injectables including depot medroxyprogesterone acetate (DMPA) it is 6%. Given the importance of avoiding pregnancy during use of known teratogenic drugs or drugs with potential teratogenic effects, the CEU recommends that in this situation, women using CHC, POP or DMPA should be advised to use additional contraceptive precautions (e.g. condoms). (Note that women using CHC or POP must not take any interacting drugs that could reduce contraceptive effectiveness).
- Use of barrier methods, withdrawal and fertility awareness methods alone is not recommended.

3.1. When is Contraception No Longer Needed?

Although a natural decline in fertility occurs with age, effective contraception is required until menopause to prevent an unintended pregnancy. However, clinical advice for women at age 55 and above is that all women can cease contraception, as spontaneous conception after this age is exceptionally rare, even in women still experiencing menstrual bleeding.

Refer to the CoSRH (FSRH) Guideline Contraception for Women Aged Over 40 Years, updated May 2025.

3.2 Considerations for females under 18 years of age

In some cases, teratogenic medicines may be prescribed in paediatrics, such as valproate for epilepsy. Parents or guardians should be informed that these are not desirable long-term treatments due to the teratogenic risk, and this discussion must be documented.

Individuals who have not yet experienced their first period are not required to follow the Pregnancy Prevention Programme (PPP). However, they and their parents or guardians should be informed of the potential future risks. Clinicians must provide a copy of the relevant patient guide and advise parents or guardians to contact the specialist or prescriber for treatment review once the individual has their first period.

The British Paediatric Neurology Association (BPNA) and the Royal College of Paediatrics and Child Health (RCPCH) have issued guidance on prescribing valproate to females under 18 years of age. The guidance is intended to support clinicians in adopting practices that help the individual as they transition from childhood through adolescence to adulthood.

Although structured around age and learning ability, the age ranges are not prescriptive. Each child and family should be assessed individually, and a tailored approach taken in line with the guidance. The same principles may also be applied when prescribing other teratogenic medicines to females under 18.

Refer to the British Paediatric Neurology Association (BPNA) and the Royal College of Paediatrics and Child Health (RCPCH) guidance: Prescribing valproate to female patients under 18 years of age, updated January 2024.

3.3 Drug Interactions

Drugs, including teratogens and herbal medicines may interact with hormonal contraceptives, and the CoSRH has developed guidance on potential drug interactions with hormonal contraceptives, based on evidence-based recommendations and good practice.

Refer to the CoSRH (FSRH) CEU Guidance: Drug Interactions with Hormonal Contraception (FSRH), published May 2022.

3.4 Referral for contraceptive advice

Appendix C details local community sexual health clinics for access to highly effective contraception, sexual health advice, and family planning support.

3.5 Pregnancy testing

The risk of pregnancy should be assessed before prescribing any teratogenic medicine.

The risk may be higher at the start of a new contraceptive method or when switching between methods. This is due to factors such as unprotected sex before initiation/insertion, unreliable use of the previous method, and/or the time required for the new method to reach full contraceptive efficacy.

Pregnancy tests performed at the start of a contraceptive method may not detect an early pregnancy resulting from unprotected sex in the previous three weeks. If there is any risk of pregnancy at initiation, a repeat pregnancy test should be performed three weeks later.

4 Original Packaging

Some teratogenic medicines must be dispensed in the manufacturer's original packaging, which often includes important warning information. Dispensers should not repackage these medicines into smaller quantities or place them in compliance aids, except in exceptional circumstances for an individual patient.

In such cases, a documented risk assessment must justify the need for alternative packaging. The dispenser must also ensure that the patient receives the original Patient Information Leaflet, which outlines the risks these medicines pose to an unborn child.

5 Prescribing alerts and audit functions

General practice systems (e.g., EMIS Web) have embedded decision-support tools, such as Ardens, and resources to help identify patients prescribed teratogenic medicines to support ongoing management. Where applicable, the completed risk assessment forms must be saved on the individual's record. The status of the risk minimisation review must be coded appropriately for all patients on teratogenic medicines.

6 References

a) FSRH Clinical Guideline: Contraception for Women Aged over 40 Years (August 2017, amended May 2025)
b) FSRH CEU Statement: Contraception for women using known teratogenic drugs or drugs with potential teratogenic effects (published February 2018), College of Sexual and Reproductive Healthcare Clinical Effectiveness Unit (CoSRH CEU)
c) Medicines, Ethics & Practice – section 3.3.11Pregnancy prevention programmes.
d) Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed? Drug Safety Update volume 12, issue 8: March 2019: 3
e) MHRA Public Assessment Report January 2021 Antiepileptic drugs: review of safety of use during pregnancy - GOV.UK

7 Resources

Risk minimisation materials such as Patient Guide, Annual Risk Acknowledgement/Awareness Form, poster and dispensing labels for individual medicine - available from Home - electronic medicines compendium (emc)

Information on drugs and pregnancy is also available from the UK Teratology Information Service (http://www.uktis.org).

8 Abbreviations

CEU	Clinical Effectiveness Unit
CHC	Combined Hormonal Contraception
CoSRH	College of Sexual and Reproductive Healthcare
Cu-IUD	Copper IUD
DMPA	Depot Medroxyprogesterone Acetate
FSRH	Faculty of Sexual and Reproductive Healthcare, now changed to College of Sexual and Reproductive Healthcare (CoSRH)
IMP	Progestogen-only implant
LARC	Long-acting reversible contraceptives
LNG-IUS	Levonorgestrel IUS
MHRA	Medicines and Healthcare products Regulatory Agency
POP	Progestogen Only Pill
SEL JMF	South East London Joint Medicines Formulary

9 Appendix A: Prescribing of VALPROATE in Primary Care (Female and Male)

MHRA have developed a range of safety and educational materials to support the implementation of the regulatory measures announced in the November 2023 National Patient Safety Alert, for organisations to have oversight and the precaution in prescribing valproate in men. They also include previous updates to product information on the risk of low birth weight in children exposed to valproate during pregnancy.

Clinical resources to support prescribing Valproate:

- Valproate reproductive risk – MHRA guidance, updated 14 July 2025, accessible via https://www.gov.uk/guidance/valproate-reproductive-risks
- Valproate Healthcare Professional Guide - Valproate- Healthcare professionals (HCPs) Guide
- Updated safety and educational materials to support patient discussion on reproductive risks (Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell▼) – Published 10 June 2025
- British Paediatric Neurology Association (BPNA) and the Royal College of Paediatrics and Child Health (RCPCH) – Joint guidance to provide recommendations about the use of valproate in female patients under 18 years of age, updated 31 January 2024
- Valproate medicines (Epilim▼, Depakote▼): contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met (Published 24 April 2018)

9.1 Valproate in male patients

- 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.

9.2 Infographics for prescribing valproate

Three infographics were published to clarify in which situations a review by two specialists may be required:

- Female patients under 55 years old
- Male patients under 55 years old
- Male and Female patients 55 years and older

9.3 Epilepsy - actions for General Practice team

Valproate is categorised as Amber 2 in the SEL JMF, as such, it will only be initiated by specialists, and the annual risk acknowledgement form must be completed by the specialists.

- Ensure **highly effective** contraception for all **women** of childbearing potential.
- Ensure the use of a **barrier** method (condoms) for **men** and an **effective** contraception for the **female partner** (of men on valproate) during valproate use and for 3 months after stopping valproate.
- Check the signed Annual Risk Acknowledgment Form and code on the system accordingly.
- Remind patients when the annual specialist review is required and refer to the specialist.
- Urgent referral (within days) for unplanned pregnancy and advise not to stop valproate until the specialist advises.
- Refer when people taking valproate are planning pregnancy and advise to continue contraception and valproate until specialist review.

10 Appendix B: Prescribing of TOPIRAMATE in Primary Care (Female patients aged under 55 years)

The use of topiramate is now contraindicated:

- in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled (for all indications)
- in pregnancy for prophylaxis of migraine
- in pregnancy for epilepsy unless there is no other suitable treatment

This follows a review by the MHRA, which concluded that the use of topiramate during pregnancy is associated with significant harm to the unborn child.

Clinical resources to support prescribing TOPIRAMATE:

- Topiramate (Topamax): introduction of new safety measures, including a Pregnancy Prevention Programme, published 20 June 2024, MHRA.
- Topiramate Healthcare Professional Guide - Prophylaxis of migraine
- Topiramate Healthcare Professional Guide - Epilepsy

10.1 Epilepsy - actions for General Practice team

Topiramate is categorised as Amber 2 in the SEL JMF, as such, it will only be initiated by specialists, and the annual risk assessment form must be completed by the specialists.

- Ensure **highly effective contraception** (all women of childbearing potential)
- Check signed Annual Risk Awareness Form and code on the system accordingly
- Remind patients when annual specialist review is required and refer to specialist
- Urgent referral (within days) for unplanned pregnancy and advise not to stop topiramate until specialist advises
- Refer women planning pregnancy and advise to continue contraception and topiramate until specialist review

10.2 Migraine prophylaxis

- Do NOT routinely refer women of childbearing potential prescribed topiramate for migraine prophylaxis for annual risk assessment.

Initiation:	**Annual Review:**
• Assess pregnancy risk and discuss enrolment in Pregnancy Prevention Programme (PPP) • Counsel as detailed in the healthcare guide and provide Patient Guide • Exclude pregnancy and arrange highly effective contraception. • Complete and sign the Annual Risk Awareness Form and give the patient a copy	• Invite patients for annual review • Continue treatment only if PPP requirements are met. • Ensure highly effective contraception (all women of childbearing potential) Ensure there is up to date, signed, Annual Risk Awareness Form and code on the system accordingly

11 Appendix C – South East London Sexual Health Clinics

Borough	Sexual Health Clinics	Service provider & details
Bexley	GP practices and pharmacies	Metro Charity (https://metrocharity.org.uk) Bexley Sexual Health (www.sexualhealthbexley.co.uk)
Bromley	Beckenham Beacon, 395 Croydon Road, Beckenham, Kent BR3 3QL Orpington Hospital, Sevenoaks Road, Orpington, Kent BR6 9JU Mottingham Community Health Clinic, 40 Kimmeridge Road, Mottingham, SE9 4LD	Bromley Sexual Health (sexualhealthbromley.co.uk)
Greenwich	Greenwich Sexual Health, 16 - 20 Market Street Woolwich, London SE18 6QR Saturday clinic is run by the GP federation based at Eltham Community Hospital	Greenwich Community Sexual Health Clinics, Oxleas Greenwich Sexual Health (https://greenwichsexualhealth.org) Greenwich GP Hubs - Weekend Sexual Health Clinic
Lambeth	Ground floor, Camberwell Sexual Health Centre, Camberwell Building, 100 Denmark Hill, London, SE5 9RS Minnie Kidd House (temporary from Monday 24 June) or Burrell Street clinic or Walworth Road clinic	Kings College Hospital • Camberwell Sexual Health Centre GSTT • Sexual Health GSTT
Lewisham	Waldron Health Centre, Second Floor, Suite 8, Amersham Vale, New Cross, London SE14 Rushey Green Clinic, 1st Floor, The Primary Care Centre, Hawstead Rd, London SE6 4JH	Lewisham and Greenwich Trust • Sexual Health Services at Lewisham and Greenwich
Southwark	• Ground floor, Camberwell Sexual Health Centre, Camberwell Building, 100 Denmark Hill, London, SE5 9RS • Minnie Kidd House (temporary from Monday 24 June) or Burrell Street clinic or Walworth Road clinic	Kings College Hospital • Camberwell Sexual Health Centre GSTT • Sexual Health GSTT
NHS – find sexual health services - https://www.nhs.uk/nhs-services/sexual-health-services/		