Implementing MHRA Valproate Monitoring Guidance for Patients in Kent & Medway

The purpose of this document is to outline the requirements necessary to implement the MHRA valproate guidance across NHS Kent & Medway.

This document may be subject to change as regulations and guidance develop further from a regional and national level. This document aims to establish good practice guidelines for clinicians in Kent & Medway.

1. The updated MHRA guidance (Jan 2024) now includes measures for **all** patients. An Annual Risk Acknowledgement Form (ARAF) should be completed, this discussion should be clearly documented in medical records and relevant correspondence.

    - 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 (*see point 5*).

    - At their next annual specialist review, women of childbearing potential and girls should be reviewed using a revised valproate Risk Acknowledgement Form, 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.

    - Due to the known significant risk of serious harm to a baby after exposure to valproate in pregnancy, these measures aim to ensure valproate is only used if other treatments are ineffective or not tolerated, and that any use of valproate is in accordance with the Pregnancy Prevention Programme (PPP).

2. The review of Valproate must be a person-centred risk minimisation process, which always respects the wishes and choices of the person and/or their carers. Every woman or person with capacity and of child-bearing potential can choose whether they take valproate and/or whether they engage with the MHRA guidance. This decision should be clearly documented in the patient's notes.
3. Patients should not be taken off a medication that is working well for them, nor should a patient feel pressured to use contraception if they have made an informed decision not to. This discussion should be clearly documented in the patient's notes.
4. This guidance does not apply to Valproate containing medicines administered in an emergency setting, this should continue to be prescribed when clinically indicated.
5. The following criteria may be considered as compelling reasons that the reproductive risks do not apply and therefore these patients may be excluded from the regulatory requirements.

Box 1: People may be considered for exclusion if they:

Are over 55 years (unless they are planning a family)
Have had a total or partial hysterectomy
Have had a bi-lateral oophorectomy or bilateral salpingo-oophorectomy (and are not considering IVF)
Have a confirmed menopause or documented no period for 12 months plus
Have been sterilised
Have another documented reason for infertility
Wish to be permanently excluded from the annual review (see point 6 below)

NOTE: Girls who have not yet started menstruating should NOT be excluded.

6. People who have been excluded from the pregnancy prevention programme should have a final ARAF recorded.

7. People of child-bearing potential with a learning disability are not automatically excluded from these regulations. Their risk of pregnancy should be considered on a case-by-case basis.

   Regardless of risk, an ARAF should be completed on at least one occasion (see point 6).

   It is recommended that at a patients annual Learning Disability Health check, it is ensured that the patient has a completed and up to date ARAF, any potential changes to the patient's pregnancy risk should be notified to the specialist prescriber.

   Should a person with a learning disability become pregnant, clinicians should use a needs-led personalised care approach, incorporating individual capacity and risk assessments and agreeing management of any identified risks. Where safeguarding concerns are identified, these should be raised through the appropriate channels and processes and managed supportively.

8. If a person's condition and circumstances are unlikely to change, it would be acceptable for the specialist to decide to annotate the ARAF to permanently exclude the patient, especially if undertaking the annual reviews are distressing for the patient/carer. The patient would no longer require an annual review; however the patient/carer should be informed to notify their healthcare professional if circumstances change.

9. If the person's risk of pregnancy in the next 12 months is considered low (See box 2) it is acceptable for the specialist to annotate the ARAF to reflect this, giving the reason.

Box 2: People with a lower risk of pregnancy include:

Woman or person is at older end of age range (45 +) (and is not planning to a family)
Woman or person is peri-menopausal
Woman or person is in monogamous relationship where partner has had a vasectomy
Sexually active exclusively with female partner(s)
Girl/woman/person not currently sexually active and unlikely to be so in next 12 months

10. If the person's likelihood of pregnancy is not low but they decline the annual review and decline the PPP, they should be provided with information on the risks to the baby in the event of pregnancy, this decision and discussion should be clearly documented. Annual reviews should continue to be offered.

11. Women and people who are of childbearing potential and sexually active or likely to be so in the foreseeable future should be offered **highly effective contraception (HEC)** as defined by the MHRA – see box 3. This should be documented. It should be recognised that this is the woman or person's choice, and the clinician should take a pragmatic view.

12. Box 3: **Highly effective Contraception**

Copper intrauterine device
Levonorgestrel intrauterine device
Progestogen only implant **
Progestogen only injection ***
'Doubling up' of two user dependent methods e.g. combined oral contraceptive plus barrier method (this is a less reliable form of contraception relying on users)

* Confirm that HEC is within manufacturer's licensed duration of use:
Intrauterine contraception (fsrh-clinical-guideline-intrauterine-contraception-mar23-amended.pdf)
Progestogen only implant (fsrh-guideline-progestogen-only-implants.pdf)
** may not be suitable if the patient is using other enzyme inducing anti-seizure medicines
** considered HEC if there is documented evidence that repeat injections have been administered on schedule.

13. If the woman or person declines highly effective contraception prescribers should clearly document discussions and decisions in clinical letters/systems. this may include sexual health clinics and community pharmacies. For some women or people, hormonal contraceptives may exacerbate their epilepsy. For some women or people with learning disability the insertion of an intrauterine device may necessitate a general anaesthetic.

14. If the decision is taken to undertake the annual valproate risk acknowledgement consultation remotely, clinicians must still ensure the form is signed by all parties and returned for this document to be official and the process completed.

Guidance on the responsibilities of Primary care clinicians

15. Primary care clinicians should ensure that all patients prescribed valproate containing medicines (sodium valproate, valproic acid and valproate semisodium) are identified and known to the practice.

16. Patients should have a copy of their up-to-date ARAF (Annual Risk Acknowledgement Form) on their GP record.

- All male patients newly started on Valproate (since January 2024) should have a completed ARAF – signed by two specialists- on their GP record.
- All female patients or people of childbearing potential should have an up-to-date copy of a revised Risk Acknowledgement Form, which will include the need for a second specialist signature if the patient is to continue with valproate.
- Female patients or people of childbearing potential will subsequently require annual reviews with one specialist unless the patient's situation changes.
- Current regulations do not require historic/existing male patients (initiated on Valproate before January 2024) to have a completed ARAF, however this may be subject to change as further research emerges on the risks of fertility to male patients. At opportune moments all male patients prescribed Valproate should be advised and informed of the fertility risks now understood to be attributed with the drug.

17. Primary care clinicians should ensure that patients of childbearing potential prescribed Valproate have a consultation around family planning and have robust PPP in place- i.e. highly effective contraception (see box 3 on page 3) (unless exceptions apply as outlined earlier in this guide- these must be clearly documented in the patient notes)

18. Patients should be provided with the MHRA Valproate Patient Guide (Link)

19. The sufficient monitoring of Valproate patients is a CQC requirement which GP practices must be shown to adhere to. A CQC inspection will include:

- Checking relevant practice staff are aware of the alert, including the most recent updates and of the risks relating to valproate.
- Reviewing the action taken to make sure affected patients have been identified, contacted, and reviewed. This will usually include checking a sample of patient records.
- Reviewing arrangements in place to check relevant actions are complete. Checking no new patients affected have joined the practice.
- The use of standardised searches to ensure alerts have been appropriately acted upon.

20. The monitoring and safe prescribing of Valproate is the responsibility of the clinician who prescribes it, regardless of whether a specialist has initiated it or not. Primary care prescribers are advised to ensure they feel competent and confident to continue prescribing and where necessary, seek assurances from the specialist.

21. Practices should make steps to ensure patients have been or are scheduled to be reviewed by a specialist in a 12-month period however, valproate **should not be** withheld from people because an ARAF has not been completed. Abrupt withdrawal of valproate can have devastating and even life-threatening consequences and in nearly all cases the valproate should be prescribed.

References:

- Valproate use by women and girls: information about the risks of taking valproate medicines during pregnancy 2023 (online) Valproate use by women and girls - GOV.UK (www.gov.uk) https://assets.publishing.service.gov.uk/media/6565ddf162180b0012ce82fd/NatPSA-2023-013-MHRA.pdf
- MHRA. Valproate use by women and girls. 2018 [online]. www.gov.uk/guidance/valproate-use-by-women-and-girls
- Pan Colleges' Guidance on valproate (2020)
- Pan_College_Guidance_Document_on_Valproate_Use V2.1.pdf (rcpch.ac.uk)
- CQC GP mythbuster 91: Patient safety alerts https://www.cqc.org.uk/guidance-providers/gps/gp-mythbusters/gp-mythbuster-91-patient-safety-alerts
- MHRA Valproate Patient Guide https://www.medicines.org.uk/emc/rmm/1204/Document