Safer prescribing of sodium valproate and valproic acid (valproate) (Female patients aged under 55 years) in Primary Care

Background

The Area Prescribing committee (APC) recommends sodium valproate (all brands and salts) for women of childbearing potential for the treatment of epilepsy or bipolar disorder, in line with the Medicines and Healthcare products Regulatory Agency (MHRA).

A National Patient Safety Alert published in November 2023 introduced a regulatory change from January 2024 stating that:

A) 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.

B) 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

The MHRA has published a set of resources, the valproate toolkit, to emphasise the need to avoid the use of valproate in girls and women of childbearing potential and warn women of the very high risks to the unborn child of valproate in pregnancy (see below Appendix 6 Useful links)

Whilst the use of valproate outside of the licensed indications has not been considered by APC, any use of valproate in women of childbearing potential irrespective of indication would be subject to the Pregnancy Prevention Programme (PPP). Link to MHRA Pregnancy Prevention Programme

Primary Care

Healthcare professionals who seek to prescribe valproate for their female patients younger than 55 years must:

- Review the patient's record to ensure they are under a specialist, that the specialist has completed with the patient all four steps of the Annual Risk Acknowledgment Form (ARAF) and that it is coded on EMIS (See Appendix 4)

(All ARAFs must be completed on revised form which will include the need for a second specialist signature for the initial/ next ARAF, thereafter 1 signature is acceptable (Appendix 6).)

- Ensure that the patient is on highly effective contraception if applicable.
- If any of this information is missing the practice must ensure this is followed up with the specialist.

If circumstances change between annual reviews referral may be necessary e.g.

- Female children who have not yet reached menarche (not started her periods) DO NOT need to fulfil the conditions of prevent, but they and their responsible person need to be aware of the risks for the future. Refer urgently when this occurs.
- If the compelling reason(s) suggesting no risk of pregnancy may be subject to change, the risks should be discussed at subsequent annual reviews or sooner if their circumstances change.

Consider adding to the instruction in certain circumstances:
'If your risk of getting pregnant changes contact your doctor.'

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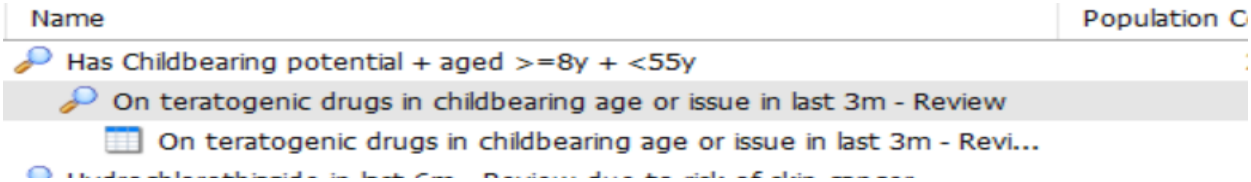
Specialist prescriber responsibilities for prescribing and annual review:

Complete the Annual Risk Awareness Form (ARAF) which includes:

- Step 1: Establish whether the patient is at risk of the reproductive harms of valproate.
- Step2: 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 (risk assessment/ awareness and acknowledgement)

The Care Quality Commission (CQC) will review compliance with the regulations for sodium valproate prescribing during inspections. Ardens CQC inspection searches are available in the safety alerts folder and Sodium valproate is one of the medicines included:



:

Warnings on use of valproate during pregnancy for bipolar disorder or for epilepsy

Prescribing valproate to a woman of childbearing potential without the pregnancy prevention programme conditions being fulfilled is contraindicated and represents an unlicensed use of the drug. Use of valproate during pregnancy for epilepsy (unless two specialists independently document that there is no other effective or tolerated treatment) and bipolar disorder, are both unlicensed. **Reference:** Booklet for Healthcare professionals: Valproate in women with childbearing potential

. This is the case even when treatment is based on an informed choice made by the patient.

Prescribers are expected to follow the General Medical Council's guidance in "Good practice in prescribing and managing medicines and devices". You must document in the patient's clinical record your reason for unlicensed use, that you have informed the patient of the unlicensed use and its associated risk.

The Medicines for Women's Health Expert Advisory Group of the Commission on Human Medicines has developed an aide-memoire table to provide guidance to prescribers of medicines with teratogenic potential on the frequency of pregnancy testing needed to avoid exposure in pregnancy during treatment, depending on the chosen contraceptive method which provides a summary of the pregnancy testing advice for the most common contraceptive methods.

Further information is available on the Surrey PAD including shared care agreements for differing conditions, links to national guidelines and MHRA advice at Surrey PAD Sodium valproate (with childbearing potential)

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Flow diagram: Summary on how to manage patients of childbearing potential on valproate within primary care.

New Patients

The specialist should prescribe a minimum of 1 month at initiation before transfer of care is requested with the patient's primary care prescriber. Primary care should only prescribe once the patient is stable, shared care has been received and signed ARAF/PPP in place (2 specialists to sign in patients <55years)

NO

If either are absent [without very detailed explanation as to why not] communicate back to consultant urgently requesting this information to enable prescriber to take over prescribing responsibility.

Existing Patients

Run report within prescribing system (See Appendix 1) to identify women of childbearing age on valproate medication

Use the Ardens template to do annual review (Appendix 2)

Ensure patient is on highly effective contraception if appropriate and document on clinical system. If prescribed outside primary care add to Hospital issue only section of medication list.
(Click **HERE** for guidance)

Has the patient had an annual specialist review including provision of Annual Risk Acknowledge Form (ARAF) completed?

All ARAFs must be completed on revised form which will include the need for a second specialist signature for the next ARAF, thereafter 1 signature is acceptable (Appendix 6).
Y/N

NO

Send referral to request an ARAF using the auto-populated referral letter on clinical system (Appendix 3) and use appropriate SNOMED code (Appendix 4)

YES

Once received, code in clinical system ARAF complete (Appx 4)

Periodically check all patients to ensure all patients on valproate have been reviewed, an ARAF filled out and on highly effective contraceptive

If on PPP but planning a family

OR

If PPP not in place and possibly pregnant

Refer URGENTLY to consultant

Prescriber needs to undertake annual review of patients to check the patient

- Understands the risks of valproate use in pregnancy
- Adheres to PPP with one highly effective or two effective contraceptive methods in place
- Has a specialist review annually to discuss risks

Prescribers should report any suspected adverse reactions associated with valproate, including adverse pregnancy outcomes, to the **Yellow Card Scheme**

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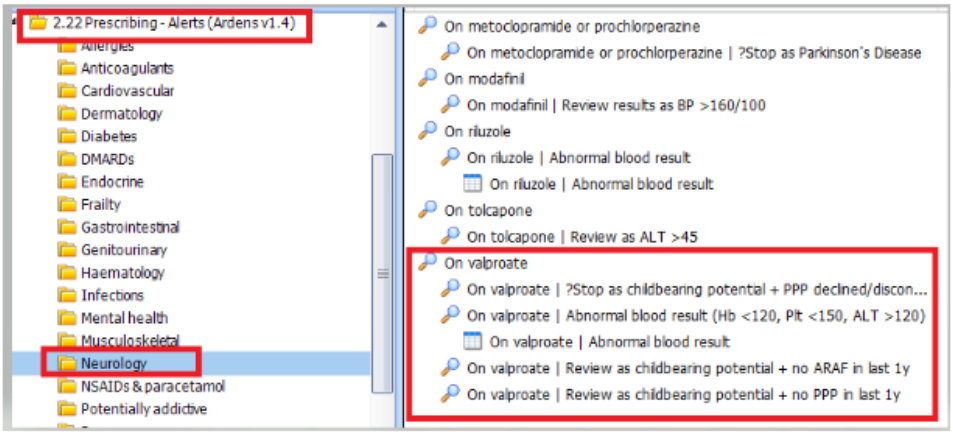
Appendix 1. Screen shot of Arden's search on EMIS and SystmOne

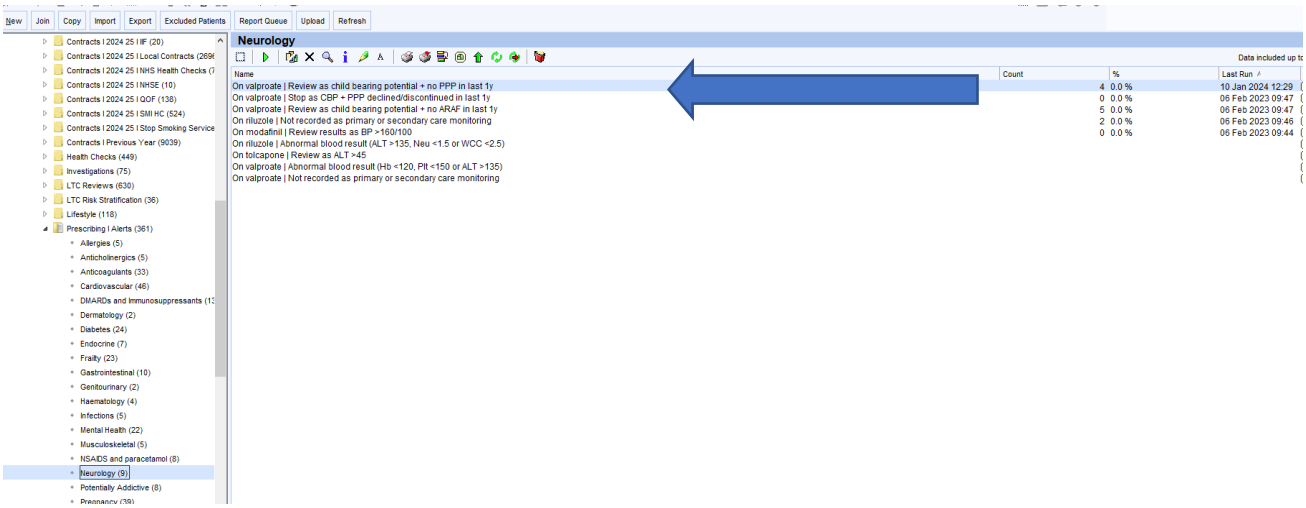
EMIS

Reference: Valproate Searches : Ardens EMIS Web

To locate these searches, navigate to the **Population Reporting** module > **Ardens Searches > 2.22 Prescribing - Alerts > Neurology** search folder.



SystmOne



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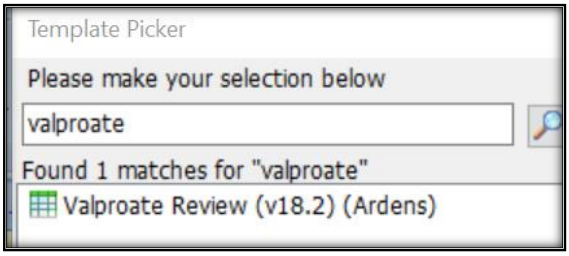
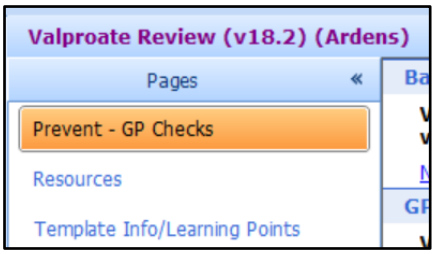
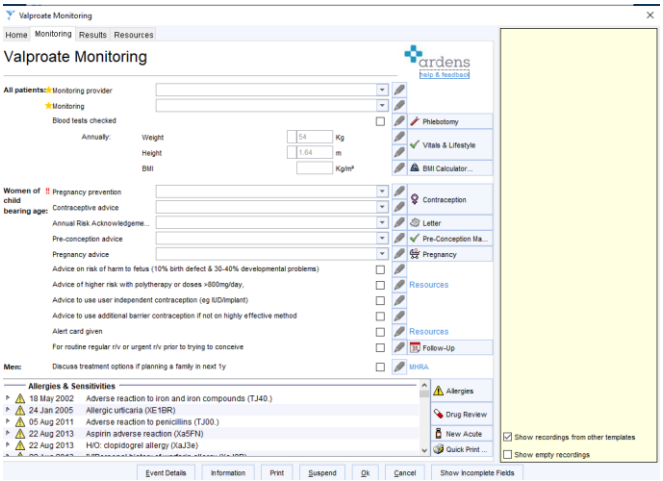
Appendix 2 Screen shot of Ardens template on EMIS and SystmOne

EMIS





SystmOne



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Appendix 3 Auto-populated referral letter on clinical system to request ARAF

GP Referral Form for Annual Review

SABP GP Referral oform for Sod Valp S´

Appendix 4 Valproate Project: SNOMED Codes

NHS Digital have released SNOMED codes for valproate. It is recommended that all practices use these codes to support the recording of a patients Annual Risk Acknowledgement Form status. These codes can be used for **ALL** patients on valproate for any condition, licensed or unlicensed, not just mental health.

• **Valproate Annual Risk Acknowledgement Form completed** (situation)
SCTID:1366401000000107
Valproate Annual Risk Acknowledgement Form completed
Valproate ARAF (Annual Risk Acknowledgement Form) completed
• **Referral for completion of Valproate Annual Risk Acknowledgement Form** (procedure)
SCTID: 1366381000000107
Referral for completion of Valproate Annual Risk Acknowledgement Form
Referral for completion of Valproate ARAF (Annual Risk Acknowledgement Form)

Advice for Healthcare Professionals: Please ensure the correct codes are used when entering information onto patients' notes

Appendix 5 Additional documents

Valproate key messages SABP FINA

Appendix 6 Useful links

There are different risk acknowledgement forms for male and female patients.

Female ARAF

Booklet for Healthcare professionals: Valproate in women with childbearing potential

Patient Card

Patient Guide: What women and girls need to know about valproate

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