Valproate pathway and guidance

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About this guidance

This guidance has been developed by the local Valproate Safety and Implementation Group consisting of the following stakeholders from the local healthcare system: Consultant Neurologists and Psychiatrists for Adults and Paediatrics, Specialist Nurses for Epilepsy, General Practitioners, Specialist Pharmacists and Pharmacy Technicians including representation from local Sexual Health Services. It is not intended to replace the Medicines and Healthcare Products Regulatory Agency (MHRA) guidance on use of valproate but provide advice on local implementation of the National Patient Safety Alert (NatPSA) for safe valproate use. Information contained in the MHRA guidance has not been replicated unless necessary for clarification.

Purpose

This pathway and guidance aim to:

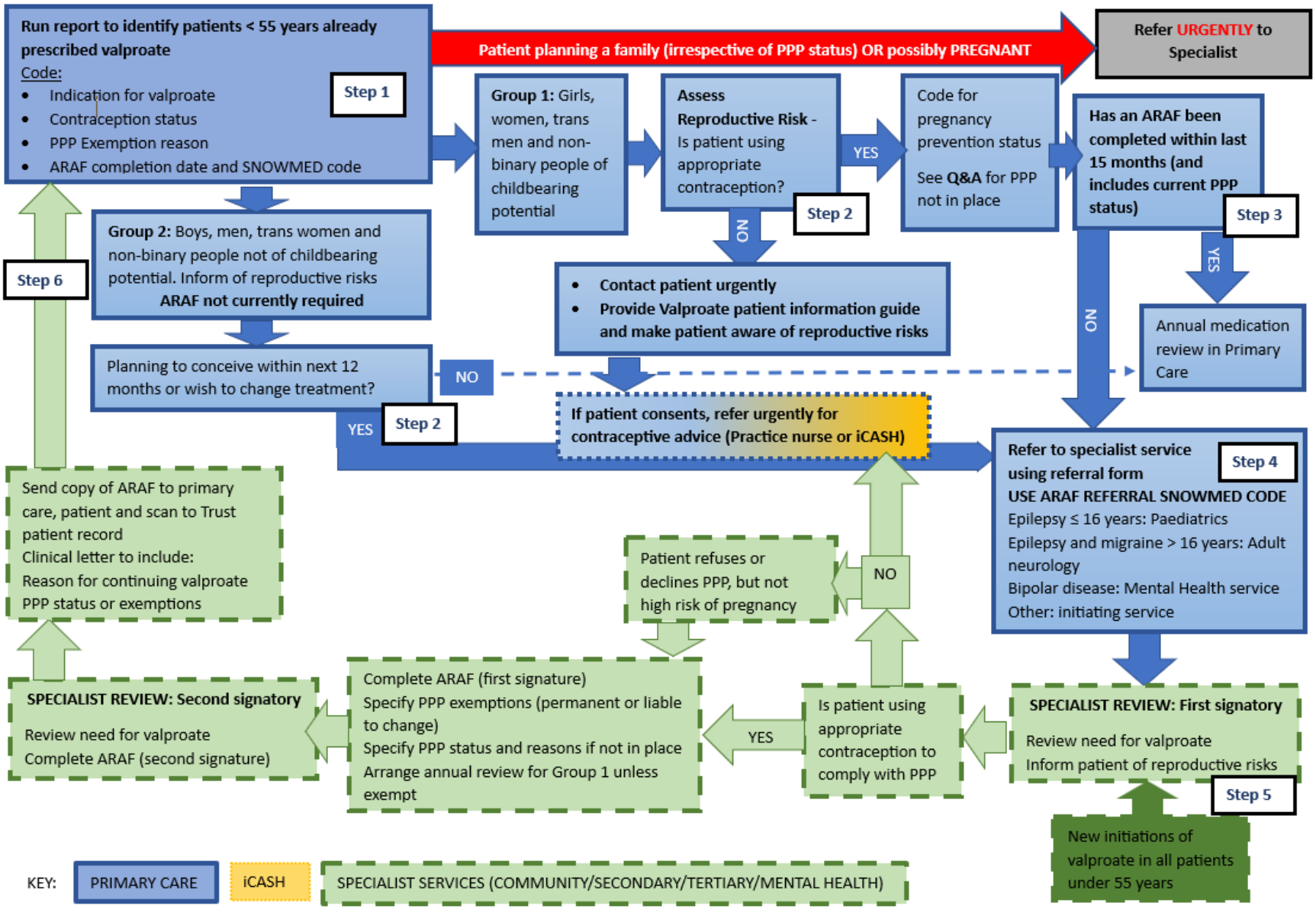
- Clarify the roles and responsibilities of clinicians involved in prescribing valproate and ensure communication between different clinicians and services.
- Recognise the shared responsibilities in supporting safe prescribing of valproate for all patients across Primary Care, Community services, Mental Health teams, Secondary and Tertiary Specialist teams and services.
- Facilitating governance and appropriate monitoring of valproate prescribing in those who may be at risk from valproate associated reproductive risks.

Key Principles

This pathway and guidance have been developed to support healthcare professionals to:

- Ensure safe prescribing of valproate and supporting appropriate use in the best interests of the patient.
- Inform those on valproate of the reproductive risks, and methods to mitigate these risks (i.e.., PPP- Pregnancy Prevention Programme)
- Ensure shared decision making with individual patients on the clinical and safe use of valproate whilst respecting patient choice.

Pathway


Run report to identify patients < 55 years already prescribed valproate
Code:
Indication for valproate
Contraception status
PPP Exemption reason
ARAF completion date and SNOWMED code
Step 1
Patient planning a family (irrespective of PPP status) OR possibly PREGNANT
Refer URGENTLY to Specialist
Group 1: Girls, women, trans men and non-binary people of childbearing potential
Assess Reproductive Risk - Is patient using appropriate contraception?
YES
NO
Step 2
Code for pregnancy prevention status
See Q&A for PPP not in place
Has an ARAF been completed within last 15 months (and includes current PPP status)
Step 3
YES
NO
Annual medication review in Primary Care
Group 2: Boys, men, trans women and non-binary people not of childbearing potential. Inform of reproductive risks
ARAF not currently required
Step 6
Planning to conceive within next 12 months or wish to change treatment?
NO
YES
Step 2
Contact patient urgently
Provide Valproate patient information guide and make patient aware of reproductive risks
If patient consents, refer urgently for contraceptive advice (Practice nurse or iCASH)
Refer to specialist service using referral form
Step 4
USE ARAF REFERRAL SNOWMED CODE
Epilepsy ≤ 16 years: Paediatrics
Epilepsy and migraine > 16 years: Adult neurology
Bipolar disease: Mental Health service
Other: initiating service
Send copy of ARAF to primary care, patient and scan to Trust patient record
Clinical letter to include:
Reason for continuing valproate
PPP status or exemptions
Patient refuses or declines PPP, but not high risk of pregnancy
NO
SPECIALIST REVIEW: First signatory
Review need for valproate
Inform patient of reproductive risks
Step 5
SPECIALIST REVIEW: Second signatory
Review need for valproate
Complete ARAF (second signature)
Complete ARAF (first signature)
Specify PPP exemptions (permanent or liable to change)
Specify PPP status and reasons if not in place
Arrange annual review for Group 1 unless exempt
YES
Is patient using appropriate contraception to comply with PPP
New initiations of valproate in all patients under 55 years
KEY:
PRIMARY CARE
iCASH
SPECIALIST SERVICES (COMMUNITY/SECONDARY/TERTIARY/MENTAL HEALTH)

Introduction

- Valproate is a medicine used in the treatment of epilepsy and bipolar disorder. It is also used to treat other conditions including migraine (off-label use).
- All healthcare professionals involved in the prescribing or monitoring of valproate must be familiar with the 'Guide for Healthcare Professionals'.
- Further regulatory changes for valproate use have been introduced by the MHRA via a National Patient Safety Alert (NatPSA) issued in November 2023 and came into effect in January 2024. These changes relate only to oral valproate preparations.
- These changes bring greater scrutiny to the prescribing of valproate in female patients of childbearing potential (under the age of 55 years old), as defined by the MHRA, including the need to have two separate specialists independently sign the required Annual Risk Assessment Form (ARAF).
- The regulatory change within the most recent alert also extends to new initiations of valproate for males under the age of 55 years old, as defined by the MHRA, being initiated on valproate need to have two specialists independently sign the required Risk Acknowledgement form (RAF).
- In February 2025, the MHRA confirmed that review by two specialists is required for initiating valproate but not required for male patients already taking valproate.
- The Commission on Human Measures advised that these measures apply to people under the age of 55 because this is the age group most likely to be affected by the reproductive risks of valproate. However, it is important to note that the risks should also be considered when prescribing to people over the age of 55 years who are planning to have children.
- Three infographics have been produced to clarify in which situations review by two specialists may be required:
    - For female patients under 55 years
    - For male patients under 55 years
    - For male and female patients 55 years and over
- All practitioners treating people taking valproate should be mindful that some individuals who do not identify as female may be of childbearing potential therefore patient groups have been defined as follows within this local guidance:
    - **Group 1 - Girls, women, trans men and non-binary people of childbearing potential (i.e. potential to fall pregnant) under 55 years of age**
    - **Group 2 – Boys, men, trans women and non-binary people not of childbearing potential aged under 55 years old.**
- Information about the reproductive risks of taking valproate medicines and the measures in place to reduce potential harm is available on the MHRA website.

MHRA Drug Safety Updates and materials

This guidance should be read in conjunction with the following MHRA Drug Safety Updates and materials:

- Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell▼): updated safety and educational materials to support patient discussion on reproductive risks - June 2025
- Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell▼): review by two specialists is required for initiating valproate but not for male patients already taking valproate - February 2025
- Valproate use in men: as a precaution, men and their partners should use effective contraception - September 2024
- Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell▼): new safety and educational materials to support regulatory measures in men and women under 55 years of age - January 2024
- Valproate: dispense full packs of valproate-containing medicines - October 2023

Step 1: Identification and review of patients prescribed valproate under 55 years

Identification of patients prescribed valproate

- Prescribing of valproate in primary care in patients should only occur under guidance from a relevant specialist and all Group 1 patients should be under a relevant specialist service if reproductive risks from valproate are present.
- Valproate should not be discontinued except on specialist advice.
- GP practices need oversight of **all** patients under the age of 55 years prescribed valproate. GP practices should use regular searches available in the GP system, SystmOne and EMIS web to identify all patients prescribed valproate.
- The GP clinical systems identify patients according to their biological sex at birth. To support with patient identification within GP practices, the following searches have been developed to identify patients prescribed valproate under 55 years of age (including acute and repeat prescriptions for the last 12 months):

1) Female patients under 55 years of age with an issue of valproate in the last 12 months
2) Male patients under 55 years of age with an issue of valproate in the last 12 months
3) Unknown gender patients under 55 years of age with an issue of valproate in the last 12 months.

- These searches include valproate preparations of all strengths and formulations including generically, and the following brands: *Belvo®, Convulex®, Depakin®, Depakote®, Dyzantil®, Epilim®, Epilim® Chrono, Epilim® Chronosphere, Episenta®, Epival®, Orlept®, Sodium valproate, Syonell® and Valproic acid.*
- For the patients identified as unknown gender (search 3) within the clinical system, GP practices will need to review and assign the individual accordingly to either group 1 or group 2.

- In SystmOne the searches can be found at: C&P GP practice group > Medicines Optimisation MOT > 11 Valproate.
- In Emis Web the searches can be found at: NHS Cambridgeshire and Peterborough CCG Search > C&P Medicines Optimisation MOT > 11 Valproate.
- Audit templates are available within the GP clinical system and from PrescQIPP to support for use in local GP practices.

Review and monitoring of valproate

- All patients prescribed valproate must have a medication review undertaken by an appropriate clinician at least annually in primary care. This must be recorded in detail within the patient's notes, ideally using the Ardens 'Valproate monitoring' template.
- Valproate is a black triangle medication; any suspected adverse reactions must be reported to the MHRA via the Yellow Card Scheme.
- The Care Quality Commission will seek assurance that the recent MHRA alert relating to valproate has been handled appropriately as part of their inspection criteria when visiting GP practices.
- Ensure **all** patients have been provided the updated patient information guide. Hard copies of this guide can be ordered via Sanofi Medicines Information department by email UK-Medicalinformation@sanofi.com or phone 0800 035 2525.

Coding and Recalls

- All GP practices must have a robust process in place for patient recall for annual reviews.
- Using the Ardens template for valproate monitoring will help to ensure the most appropriate read codes are used. Table 1 below includes recommended read codes for safe valproate prescribing and monitoring.
- To aid with effective recalls and referral to appropriate specialist services, patients must be appropriately read coded so they can be quickly identified. This includes read codes, as applicable, to indicate:
    - Indication for valproate
    - That a completed and valid Risk Acknowledgement Form (including date) is in place, or a referral has been made for completion
    - Contraception status (PPP started/declined or not needed)
    - Conditions for which the patient is exempt from the PPP (PREVENT) and completion of an ARAF is not required (see Step 2 and Frequently Asked Questions (FAQs) document).

Table 1 – Clinical system recommended coding for safe prescribing and monitoring of valproate

Clinical system coding	SystmOne code	SNOMED Concept ID
Valproate Annual Risk Acknowledgement Form completed *To be used when Valproate ARAF or RAF received from secondary care [date of ARAF or RAF to be inserted into the GP clinical record]*	Y362e	1366401000000107
Referral for completion of Valproate Annual Risk Acknowledgement Form *To be used when a referral is made from primary care to secondary care [date of referral to be inserted into the GP clinical record]*	Y38a6	1366381000000107
Pregnancy Prevention Programme started *To be used when an ARAF is received from secondary care and ongoing annual reviews are required.*	Y2f16	1129771000000103
Pregnancy Prevention Programme declined *To be used when ARAF is received from secondary care and ongoing annual reviews **are** needed, for example patient of childbearing potential in sexual relationship that cannot result in pregnancy (for example same sex relationships) **or** patient declines due to religious or social grounds. It should be clearly documented who has declined the PPP, whether this is the patient, or whether this decision has been made by a parent or caregiver, where appropriate.*	Y2f17	112980100000100
Pregnancy Prevention Programme not needed *To be used when ARAF is received from secondary care and ongoing annual review will be needed in the future, for example a patient of childbearing potential who has not yet reached menarche.* *To be used when ARAF is received from secondary care and ongoing annual reviews are **not** needed as there is a permanent reason that a pregnancy prevention programme is not needed, for example, a patient of childbearing potential has had a hysterectomy.*	Y2f18	1129791000000104

Step 2 Assessment of Reproductive risks, Contraception and Compliance with Pregnancy Prevention Programme

- It is the responsibility of prescribers in Primary Care, to ensure that for patients in group 1 under 55 years with childbearing potential, the conditions of the Pregnancy Prevention Programme (PPP or sometimes called PREVENT) are met. The FAQs document provides further advice on situations where PPP does not apply or a patient chooses not to follow PPP).
- Primary care and community services should support in expediting access to contraception for those on valproate or those in whom valproate is being considered (as advised by specialist).
- Where a patient is seen by community sexual health services for contraception, patient consent to share this information with patient's GP and specialist services should be sought.
- For patients in group 2 under 55 years, it is important that these patients are given advice about the possible risk of neurodevelopmental conditions in children of group 2 patients taking valproate at conception. They should be counselled that if they wish to plan a family in the 12 months or wish to consider changing treatment that they discuss this with their healthcare professional. It is recommended that group 2 patients use effective contraception (condoms, plus contraception used by their 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.
- Any patient who wishes to consider changing their treatment should be referred to their specialist team for a routine review.

Assessment of Reproductive risks

The following reproductive risk assessment table is to support primary care clinicians in assessing the potential reproductive risk for individual patients and can be used as a guide for supporting appropriate referrals to specialist teams. The specialist teams will also be using these criteria for prioritisation of patient appointments.

Table 2 - Priority for referral based upon reproductive risk assessment

Reproductive risk assessment	Group 1 patients	Priority for referral	Group 2 patients	Priority for referral
High risk	• No contraception and sexually active • Actively trying to conceive	**Urgent**	Actively trying to conceive	**Urgent**
Moderate risk	• Barrier methods	Routine	• Barrier methods	N/A

Reproductive risk assessment	Group 1 patients	Priority for referral	Group 2 patients	Priority for referral
Low -Moderate risk	• User dependent hormonal contraception	Routine		N/A
Low risk	• LARC prescribed • Patients in a sexual relationship which could not result in pregnancy (e.g., same sex relationships or established male partner with vasectomy). • Not in a sexual relationship on religious or social grounds	Routine		N/A
No risk	• Hysterectomy • Bilateral oophorectomy • Post-menopausal • Infertility from another cause (not seeking fertility treatment).	Only needs referral if ARAF for exemption has not been completed.	• Male vasectomy • Infertility from another cause	N/A

Effective Contraception and Pregnancy Prevention Programme (PPP also called PREVENT)

- The use of contraception must be discussed and the patient's understanding of the importance of its use whilst prescribed valproate checked.
- It is important to be sensitive to the patient's individual situation and circumstances about contraception use and a shared decision-making approach should be used. All patients should be supported and provided with usual care, irrespective of their individual decisions on PPP or continuation of valproate.
- Highly effective contraceptive methods should be used, where possible, all of which have a failure rate of less than 1% with typical use. This includes the long-acting reversible

contraceptives (LARCs) copper intrauterine device, levonorgestrel intrauterine system and progestogen-only implant.

- Some group 1 patients do not wish, or it is not clinically appropriate to use LARC. Other contraceptive methods described as *effective* include combined hormonal contraceptives (pills, patches or vaginal rings) and progestogen-only pills and injectables, which have typical-use failure rates of 6-9%. If *effective* methods are used then an *additional barrier contraception*, such as condoms, are advised and pregnancy testing considered, as applicable, for example if concerns relating to compliance with contraception. The NHS England Valproate Decision Making tool may help patients in deciding choice of contraception and effectiveness.
- It is imperative to ensure that the **renewal of contraception is not delayed** for patients taking valproate.
- *It is important to avoid any interacting drugs that could reduce contraceptive effectiveness.* If there are any concerns regarding contraceptive options and drug-drug interactions, further information can be found in the British National Formulary (BNF). The relevant specialist service can also be contacted for advice as needed.
- Where effective contraception is not in place, is clinically needed and the patient is willing to commence contraception, **an urgent referral must be made for contraception** to be initiated with either the practice nurse or to sexual health services (see referral form within the GP clinical system). The importance of abstaining from sexual intercourse or the interim use of two effective contraception methods must be discussed and documented.
- The PPP status of the patient must be read coded within the patient notes (see Table 1).
- There may be circumstances where group 1 patients taking valproate do not want to use effective contraception and are fully informed of the risks of becoming pregnant whilst taking valproate, particularly those at low reproductive risk.
- Please see FAQs document for further advice on clinical circumstances where patients do not wish to use contraception and are prescribed valproate, as well as the need to ensure repeat prescriptions of Valproate are not withheld.

Exemptions from Pregnancy Prevention Programme

- Contraception may not be required where the chance of pregnancy is deemed low, for example following female sterilisation, hysterectomy, or in sexual relationships where conception is not biologically possible (e.g., same-sex relationships not seeking fertility treatment).
- In situations involving individuals who may lack capacity to consent to sexual activity such as those with significant intellectual disability, decisions should be made in line with the Mental Capacity Act (2005) and safeguarding principles, rather than on the basis of disability alone.
- Where effective contraception is not considered necessary as the individual patient reproductive risk is low, the reasons for this must be appropriately read coded within the

patient notes (noting which healthcare professional has identified this) and clearly documented on the ARAF by the prescribing specialist. The specialist should clearly document on the ARAF whether the circumstances are considered permanent, and the patient is subsequently excluded permanently from the PPP or whether there is a need to review the PPP on an annual basis.

Patients who wish to conceive or suspected pregnancy whilst taking valproate (See FAQs document)

- MHRA guidance acknowledges that there may be patients who may still conceive on valproate for epilepsy, if two specialists agree that other treatments have not been effective or tolerated for their condition. Valproate is contra-indicated in pregnancy for the treatment of bipolar disease. If pregnancy is confirmed, urgent discussion should take with the specialist who will review the patient as soon as possible to discuss treatment options.
- All group 1 patients must be reminded that where pregnancy is suspected or the patient is planning a pregnancy, to report this urgently to their GP so that an urgent referral can be made to their specialist. The patient must be reminded to continue to take their valproate as prescribed.
- Where there is a risk of pregnancy, a serum pregnancy test must be offered at least 14 days after the last possible date on which the patient had or could have had unprotected sexual intercourse or sexual intercourse without effective contraception in place.
- Valproate should not be discontinued, even if the patient stops contraception, before urgent specialist review.
- It is the responsibility of the specialist to review whether continued treatment with valproate remains in the patient's best interests during pregnancy. The risks and benefits — including the potential destabilisation of the patient's condition if valproate is stopped or switched to an alternative treatment — must be fully discussed with the patient.
- If, following shared decision-making, the specialist and patient agree that the risks associated with withdrawing valproate are greater than the reproductive risks to the foetus, valproate should continue to be prescribed. The patient must not be denied usual NHS care or penalised for their decision to conceive while taking valproate.

Step 3 Risk Acknowledgement Forms

Group 1 patients

- The recent regulatory changes require that **all patients in group 1 (girls, women, trans men and non-binary people of child bearing potential) under 55 years of age** newly initiated on valproate to have an ARAF signed by two specialists. Those already prescribed valproate must have an updated ARAF form completed at their next specialist annual review.

- Where there remains a risk of pregnancy, the specialist must continue to review these patients at least annually.
- Group 1 patients currently exempt from the PPP or who have a permanent reason (e.g. post-menopausal or those after hysterectomy) why pregnancy risk is not present with a previous completed ARAF form do **not** need an updated ARAF signed by two specialists. This includes patients no longer under specialist care.

Group 2 patients

- In line with regulatory measures, a Risk Acknowledgement form (RAF) is now required only for new initiations of valproate in **all patients in group 2 (boys, men, trans women and non-binary people not of childbearing potential)** under the age of 55 years confirming that two specialists consider that there is no other effective or tolerated treatment or the reproductive risks do not apply.
- The specialist must document any exemption on the RAF and this reason should be read coded appropriately within the GP clinical system.
- In group 2 patients newly initiated on valproate, the RAF form only needs to be completed at the point of initiation of valproate. The patient's specialist will provide advice to the patient to contact GP if their individual reproductive risk status alters or if the patient wishes to plan a family.
- Group 2 patients newly initiated on valproate who have a permanent reason that they may not conceive only need one specialist signatory for the RAF.
- Copies of the completed initiation RAF must be sent to the GP practice, the patient and a copy retained in the patient's notes.
- Group 2 patients already prescribed valproate do not require a RAF and review by two specialists.
- All Group 2 patients prescribed valproate must be offered an annual medication review with appropriate monitoring undertaken in primary care.

Reviewing and recording Risk Acknowledgement Forms

- Check to ensure an ARAF or RAF completed by the patient's specialist is present, as relevant, and has been read coded within the patient notes (see Table 1)
- Where an ARAF is not completed, a referral should be made to the patient's specialist with priority for referral based on the individual patient's reproductive risk assessment (see Table 2).
- If a previous ARAF needs annual review and is overdue by more than three months, contact the patient's specialist via Advice and Guidance to check that the review is forthcoming.
- Completed forms must be uploaded and coded onto the patient management system once received. Forms should be checked to ensure the patient has also signed in the designated

box before uploading unless the specialist states that a remote consultation has taken place.

- It is also suggested that where valproate is listed as a repeat prescription item and an ARAF is required, the date of the ARAF is recorded in the script notes. The expiry date for any repeat templates of valproate should be set to the month the ARAF expires as a prompt for annual review.

Step 4: Referral to specialist services

- **Urgent referral to the patient's specialist** is required for those patients identified as **high reproductive risk:**
    - **Patient is pregnant or is actively planning a family**
    - **Patient is not using contraception where PPP (PREVENT) should apply (Group 1 patients who are not exempt from PPP) and not previously had specialist review to discuss reproductive risks of valproate**
- Where a referral is needed for completion of an up to date ARAF or if the patient is not considered of high reproductive risk, a routine referral should be made.
- Any referrals made to specialist services for completion of ARAF should be made using the referral forms available in the GP clinical system.
- Where patients are not recorded as known to secondary care services through review of their GP clinical record, or have previously been discharged, it is essential to include any previous medication history relevant to indication for valproate and any previous information available about diagnosis of condition for the referring clinician.
- Any referral to secondary care, should be clearly documented in the patient's clinical record in primary care.
- Where a referral is made for completion of ARAF this should be coded in the patient's clinical record (See Table 1).

Step 5: Review of patient by specialist services

- Specialist teams will:
    - Prioritise patients referred according to the reproductive risk assessment that is undertaken by primary care.
    - Provide advice to individual patients to contact GP if their individual reproductive risk status alters or if becomes pregnant.
    - Send copies of the completed ARAF / RAF to the GP practice, the patient and a copy retained in the patient's notes.
- The relevant provider Trust will have in place a robust mechanism in place for reviewing patients taking valproate, completing ARAF/RAF including second specialist signature and to recall patients on an annual basis, where required.

- The relevant provider Trust will also provide a clinical letter to the patient's GP practice to accompany the ARAF, with the outcome of shared decision making that will allow the following outcomes to be coded in the primary care record:
    - Indication for use
    - ARAF Completed and date
    - PPP status including reason for exemption if applicable
    - Outcome of decision for valproate prescribing
- There may be situations where the specialist agrees to continue use of valproate, even when the recommendations within the PPP (PREVENT) are not fully complied with. Careful consideration of shared decision-making and the actual risk will be reviewed on an individual basis. Examples of such clinical circumstances are available in the FAQs document.
- If there are any concerns regarding ongoing prescribing of valproate, the specialist and primary care clinician should come to a shared joint decision in the best interests of the individual patient, considering individual reproductive risks, individual choices and the patient individual responsibility and autonomy. No patient should be taken off valproate without their consent.

Patient review pathways for each clinical speciality are included within the tables below.

Table 3. Neurology Services Review Pathway – Adults with epilepsy

Patient groups	*Referral Pathway*	*First Signatory*	*Second Signatory*	*Follow up ARAF*
Group 1 and Group 2: New initiations of valproate - for patients whose seizures are not under control with Levetiracetam and Lamotrigine (+/- benzodiazepines)	**Refer to Epilepsy Clinic**: - North West Anglia NHS Foundation Trust (NWAFT) - Cambridge University Hospitals NHS Foundation Trust (CUHFT) - Outside of local geography may include (not limited to) West Suffolk NHS Foundation Trust, The Queen Elizabeth Hospital King's Lynn NHS Foundation Trust and East Suffolk and North Essex NHS Foundation Trust	**Consultant Neurologist within Epilepsy Team or Epilepsy Nurse specialist (Non-Medical Prescriber) if permanent exemption from PPP**: - Completes ARAF and decision template - Arranges second signatory - Sends dual signed ARAF to GP to commence valproate - Ensures appropriate follow up	**Consultant Neurologist or Chair of Epilepsy Multidisciplinary Team (MDT):** - Completes ARAF and decision template - Returns to first (primary) specialist	**Group 1 patients:** - Epilepsy Nurse Specialist (Non-Medical Prescriber) or Consultant Neurologist (single signatory only required) **Group 2 patients:** not needed
Group 1 only: Existing patients on valproate who are seizure free – all epilepsy types	**Local referral to General Neurology**	**Consultant Neurologist or Epilepsy Nurse Specialist (Non-Medical Prescriber) within Epilepsy Team**: - Completes ARAF and decision template - Arranges second signatory - Sends dual signed ARAF to GP to commence valproate - Ensures appropriate follow up	**Consultant Neurologist or Chair of Epilepsy Multidisciplinary Team (MDT):** - Completes ARAF and decision template - Returns to first (primary) specialist	**Group 1 patients:** - Epilepsy Nurse Specialist (Non-Medical Prescriber) or Consultant Neurologist (single signatory only required) **Group 2 patients:** not needed

Patient groups	*Referral Pathway*	*First Signatory*	*Second Signatory*	*Follow up ARAF*
Group 1 and Group 2 with reproductive risks from valproate: Existing patients on valproate who are* not *seizure free	**Refer to Epilepsy Clinic (as above)**– may be local arrangements for those under Epilepsy Nurses with Consultant Neurologist supervision	**Consultant Neurologist within Epilepsy Team**: - Completes ARAF and decision template - Arranges second signatory - Sends dual signed ARAF to GP to commence valproate - Ensures appropriate follow up	**Consultant Neurologist or Chair of Epilepsy Multidisciplinary Team (MDT):** - Completes ARAF and decision template - Returns to first (primary) specialist	**Group 1 patients:** - Epilepsy Nurse Specialist (Non-Medical Prescriber) or Consultant Neurologist (single signatory only required) **Group 2 patients:** not needed
Group 1 and Group 2: Existing patients on valproate who wish to conceive	**Refer to Epilepsy Clinic (as above)**	**Consultant Neurologist within Epilepsy Team**: - Completes ARAF and decision template - Arranges second signatory - Sends dual signed ARAF to GP to commence valproate - Ensures appropriate follow up	**Consultant Neurologist or Chair of Epilepsy Multidisciplinary Team (MDT):** - Completes ARAF and decision template - Returns to first (primary) specialist	**Group 1 patients:** - Epilepsy Nurse Specialist (Non-Medical Prescriber) or Consultant Neurologist (single signatory only required) **Group 2 patients:** not needed

Table 4. Neurology Services Review Pathway – Children with epilepsy

Patient groups	*Referral Pathway*	*First Signatory*	*Second Signatory*	*Follow up ARAF*
Group 1 and Group 2: New initiations of valproate - for patients for whom there are no other effective or tolerated options to prescribe or are within BPNA recommendations for first line use of valproate	**Refer to Epilepsy Clinic**: - In CPICS this would be North West Anglia NHS Foundation Trust (NWAFT) / Cambridge University Hospitals NHS Foundation Trust (CUHFT) / The Queen Elizabeth Hospital King's Lynn NHS Foundation Trust	**Consultant paediatrician** Completes ARAF and decision template - Arranges second signatory - Sends dual signed ARAF to GP to commence valproate - Ensures appropriate follow up	**Consultant paediatric neurologist/ Paediatrician with Expertise in Epilepsy / Epilepsy Specialist Nurse (there is NO requirement for Epilepsy Specialist Nurse to be a prescriber but must not be line managed by first signatory):** - Completes ARAF and decision template - Returns to first (primary) specialist	**Group 1 patients:** - Epilepsy Nurse Specialist (Non-Medical Prescriber) or Consultant Paediatrician (single signatory only required) **Group 2 patients:** not needed
Group 1 only: Existing patients on valproate - *all* epilepsy types	Remain under epilepsy clinic	**Consultant paediatrician:** - Completes ARAF and decision template - Arranges second signatory - Sends dual signed ARAF to GP to commence valproate - Ensures appropriate follow up	**Consultant paediatric neurologist/ Paediatrician with Expertise in Epilepsy / Epilepsy Specialist Nurse (there is NO requirement for Epilepsy Specialist Nurse to be a prescriber but must not be line managed by first signatory):** - Completes ARAF and decision template - Returns to first (primary) specialist	**Group 1 patients:** - Epilepsy Nurse Specialist (Non-Medical Prescriber) or Consultant Neurologist (single signatory only required) **Group 2 patients:** not needed

Table 5. Mental Health Services Review Pathway – Adults

Patient groups	*Referral Pathway*	*First Signatory*	*Second Signatory*	*Follow up ARAF*
Group 1 and Group 2: New initiations of valproate For the treatment of bipolar disorder where other treatments have not been effective or tolerated Other indication to be specified by the initiating specialist	**NOT referred in as initiated <u>within</u> Adult Locality Teams** - Cambridge (CALT) - Fenland (FALT) - Huntingdon (HALT) - Peterborough (PALT) **and specialist services** - CAMEO (Early Intervention Services) - Forensics - Perinatal - Learning Disability - PDCS (Personality Disorder Community Service) - Eating Disorder **and Inpatients**	**Consultant Psychiatrist of the initiating team** - Completes ARAF (Group 1) and RAF (Group 2) and decision template - Arranges second signatory - Sends dual signed ARAF/RAF to GP to commence valproate and a copy retained in the patient's notes - Ensures appropriate follow up	**Consultant psychiatrist /speciality doctor/ Specialist nurse prescriber/specialist pharmacist** - Completes ARAF (Group 1) and RAF (Group 2) and decision template - Returns to first (primary) specialist	**Group 1 patients:** - Consultant Psychiatrist/ Specialty doctor/ specialist nurse prescriber (single signatory only required) **Group 2 patients:** not needed
Group 1 and Group 2 with reproductive risks from	**Routine referral to PCMHS via eRS**	**Consultant Psychiatrist**	**Consultant psychiatrist /speciality doctor/ Specialist nurse**	**Group 1 patients:** - Consultant Psychiatrist/ Specialty doctor/

Patient groups	*Referral Pathway*	*First Signatory*	*Second Signatory*	*Follow up ARAF*
valproate: Existing patients on valproate For the treatment of bipolar disorder where other treatments have not been effective or tolerated *Other indication – primary care to specify indication on referral proforma (refer in to initiating service)* *For those with dual indication-*		- Completes ARAF (Group 1) and RAF (Group 2) and decision template - Arranges second signatory - Sends dual signed ARAF/RAF to GP to confirm ongoing prescribing of valproate and a copy retained in the patient's notes - Ensures appropriate follow up	**prescriber/specialist pharmacist** - Completes ARAF (Group 1) and RAF (Group 2) and decision template - Returns to first (primary) specialist	specialist nurse prescriber (single signatory only required) **Group 2 patients:** not needed

Patient groups	*Referral Pathway*	*First Signatory*	*Second Signatory*	*Follow up ARAF*
refer to the initiating speciality				
Group 1 and Group 2: Existing patients on valproate who have become pregnant, who wish to conceive, or consider changing treatment.	**Urgent referral to Adult Locality Team or other specialist team who initiated Valproate** **Urgent referral to Perinatal MH team for those who have become pregnant or wish to conceive** - Following urgent review by GP to ensure patient has been informed of reproductive risks and commenced on folic acid 5mg a day	**Consultant Psychiatrist** *- Taken into consideration that valproate is contra-indicated in pregnancy for the treatment of bipolar disorder.* *- Discuss suitable alternative treatment* - Completes ARAF (Group 1) and RAF (Group 2) and decision template - Arranges second signatory - Sends dual signed ARAF/RAF to GP to inform shared decision regarding prescribing of valproate - Ensures appropriate follow up	**Consultant psychiatrist /speciality doctor/ Specialist nurse prescriber/specialist pharmacist** - Completes ARAF (Group 1) and RAF (Group 2) and decision template - Returns to first (primary) specialist	**Group 1 patients:** - Consultant Psychiatrist/ Specialty doctor/ specialist nurse prescriber (single signatory only required) **Group 2 patients:** not needed

Step 6: Continuation of valproate in Primary Care

- On receipt of a completed ARAF or RAF from secondary care with corresponding clinical letter for the individual patient, primary care should ensure that the patient has the appropriate read codes in place to support (use Ardens template) rapid identification of patients as needed (see Table 1).

Roles and responsibilities of healthcare professionals involved in the prescribing, dispensing and monitoring of patients taking valproate (under 55 years of age)

Primary Care responsibilities

- All healthcare professionals involved in the prescribing or monitoring of valproate must be familiar with the MHRA alerts for valproate and have read the Guide for Healthcare Professionals.
- To have clear oversight of all patients prescribed valproate including those under the age of 55 years, regardless of childbearing potential.
- Discuss the reproductive risks with the patient and ensure that all patients have been provided the updated Patient Guide.
- Run regular audits to ensure that patients under the age of 55 years with childbearing potential meet the conditions of the PPP (PREVENT) including contraception where clinically appropriate.
- Run regular audits to ensure that all patients under the age of 55 prescribed valproate are offered advice regarding the reproductive risks and what to do if they wish to start planning a family.
- Ensure accurate and detailed recording and coding of the patient's clinical condition, reproductive risks and any known exemptions to the PPP (PREVENT) where applicable, risk acknowledgement forms and reviews undertaken.
- Ensure that valproate monitoring is undertaken and the relevant Ardens template is used to aid appropriate recording within the patient's clinical record.
- Refer patients for review into secondary care according to their individual reproductive risks using the referral form (available in GP clinical system) if an ARAF has not been completed or send Advice and Guidance for those with ARAF completed more than 15 months previously requiring annual review.
- Remind all group 1 patients that they will need to see their specialist at least annually (unless considered permanently exempt from annual review) whilst taking valproate.
- Expedite access to contraception where needed for patients of childbearing potential as clinically appropriate.
- Exclude pregnancy in patients of childbearing potential (by serum pregnancy test) before the first prescription is issued for those newly prescribed valproate.
- Remind the patient's responsible person to contact you, once the patient using valproate experiences their first period (menarche), where applicable. You will need to refer the patient back to their specialist for review (if not already under specialist review).
- If a patient becomes pregnant, inform the patient to continue their valproate treatment and urgently refer (within days) the patient to their specialist who is managing their condition.
- Work jointly and collaboratively with specialist and community services to support the safe use of valproate in patients, based on principles of shared decision making without judgement.

Specialists' responsibilities

- Discuss the reproductive risks with the patient (or parent/caregiver/responsible person).
- Exclude pregnancy in patients of childbearing potential (by serum pregnancy test) before the first prescription is issued for those newly prescribed valproate.
- Ensure highly effective contraception is in place for patients of childbearing potential before the first prescription is issued (refer to primary care or directly to sexual health services (iCASH)).
- Complete the ARAF for group 1 patients of childbearing potential and RAF for new initiations in valproate in group 2 patients, with the patient (or parent/caregiver/ responsible person); give them a copy and send a copy to the GP.
- See the patient urgently (within days) if referred in case of unplanned pregnancy or if as soon as possible patient actively wishes to plan a pregnancy.
- Provide a copy of the Patient Guide to the patient (or parent/caregiver/responsible person).
- Work jointly and collaboratively with Primary Care and community services to support the safe use of valproate in patients, based on principles of shared decision making without judgement.

Pharmacy Responsibilities

- Ensure the Patient Card is provided every time valproate is dispensed.
- Ensure the patient has received the Patient Guide or knows they can access it online using the QR code on the package leaflet.
- Confirm with patients that they have been made aware of the reproductive risks.
- Confirm with patients of childbearing potential that they have been made aware to always use effective contraception and to see their General Practitioner (GP) to be urgently referred to their specialist, should they be planning a pregnancy.
- Confirm with patients that they have been made aware not to stop valproate unless advised to do so by their specialist.
- Confirm with patients of childbearing potential to immediately contact their GP for an urgent referral to their specialist in case of suspected pregnancy.
- Dispense valproate in the original package. In exceptional circumstances, where a patient needs to receive their medication in different packaging such as a Monitored Dosage System, provide a copy of the package leaflet, the patient card and add a valproate warning sticker to the outer box.
- If a patient of childbearing potential reports that:
    - They are not continuously using an effective method of contraception,
    - They are not aware of the need for contraception, or they have not been seen by their specialist in the past year,

  dispense their medicine and refer them to their GP (contact the GP if necessary).

Sexual Health Services Responsibilities

- Expedite access to contraception for patients taking valproate, both those patients in whom valproate is planned as a new initiation, or those patients whose contraception is due to expire.
- Proactively seek consent from the patient to share information about their contraceptive choices with their GP and specialist
- Inform the patient's GP and specialist urgently where there are any concerns in relation to contraception use and attempt to delay withdrawal of contraception (with patient consent) until the GP and specialist have had the opportunity to discuss reproductive risks of valproate with the patient.

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