North Central London
Joint Formulary Committee

Minimising the teratogenic risk of valproate to patients of childbearing potential in NCL

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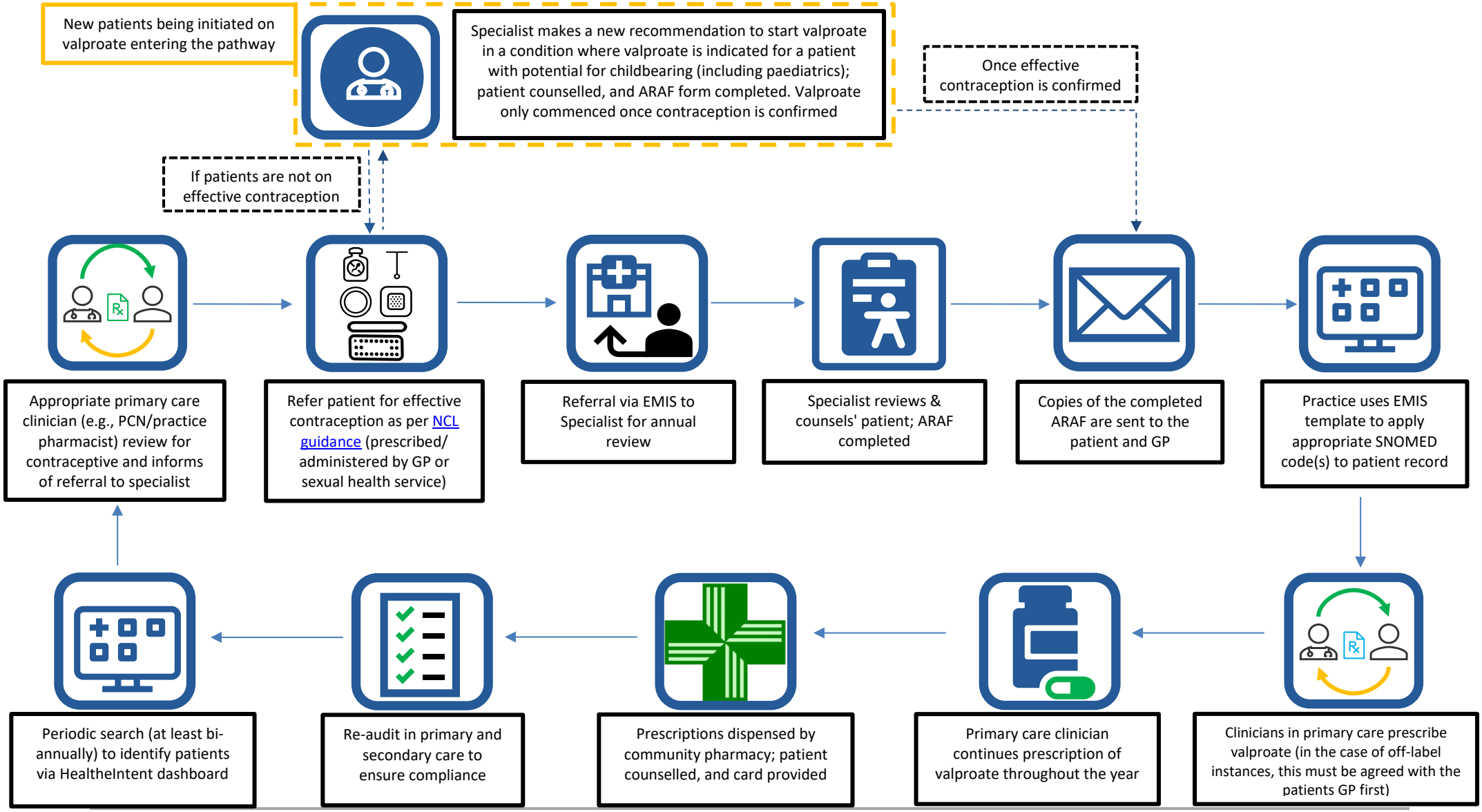
Figure 1 – Best practice pathway for patients prescribed valproate in North Central London



1. Target audience

This guidance is aimed at all sectors of healthcare, for all healthcare professionals who are involved in the health and care of patients of childbearing potential who are prescribed valproate. The entirety of this guideline applies to patients who reside within North Central London (NCL); however, certain digital technologies and developments may not currently be available to regions outside of NCL. Where digital technologies are not available, primary care teams should ensure that they develop local systems to ensure patients are referred to their specialist in a timely manner for their annual review of valproate, in line with national guidance.

2. Purpose

This guidance outlines the roles and responsibilities for the healthcare professionals involved in the management of people of childbearing potential who are (i) prescribed a valproate-based medicine; and (ii) the patient either resides within NCL and/or their specialist service is within NCL; and (iii) the patient falls within the remit of the valproate pregnancy prevention programme (named PREVENT). This guidance also aims to lay out the practical steps needed to manage patients and minimise the teratogenic risk of valproate.

3. Abbreviations and terminology

ARAF – The 'Annual Risk Acknowledgement Form', should be completed by the specialist at least annually for patients with childbearing potential.

PREVENT – The term given to the valproate pregnancy prevention programme.

'Highly effective' contraception – The term given for user independent forms of contraception, which carry <1% risk of pregnancy.

LARC – Long-acting reversible contraception

IUD – Intrauterine Device

Cu-IUD – Copper Intrauterine Device

LNG-IUS – Levonorgestrel Intrauterine System

IMP – Progestogen-only implant

COC – Combined Oral Contraceptives

POP – Progestogen-Only contraceptive Pill

DMPA – Depot Medroxyprogesterone Acetate (a form of progesterone injection)

HealtheIntent – an electronic population healthcare platform utilised in NCL

Patients with "childbearing potential" – A person who can become pregnant, who is of childbearing age, and does not have a temporary or permanent absence of pregnancy risk. This includes women and girls of childbearing age, and trans men who are biologically able to be pregnant.

4. Introduction

Valproate is a medication used to treat all forms of epilepsy, mental health disorders (including bipolar disorder and depression), migraine prophylaxis and pain management. It is an active ingredient licensed under several brand names (Epilim®, Depakote®, Convulex®, Episenta®, Epival®, Kentilim®, Orlept®, Syonell®, Valpal®, Belov®, Dyzantil® and generic sodium valproate). Valproate is associated with a significant risk of physical birth defects (10%) and neurodevelopmental disorders (30-40%) in children born when valproate was taken during pregnancy.

Since its introduction in 1974, the risks to unborn children have been increasingly understood and consequently the prescribing warnings have been strengthened (coinciding with several MHRA alerts).[1] In recent times, valproate has been the subject of the 'First Do No Harm' report[2] which outlines the history of valproate use and describes the impact on patients who took valproate whilst pregnant. In 2018, valproate became **contraindicated** in people of childbearing potential unless they meet the conditions of a Pregnancy Prevention Programme (PPP, also known as 'PREVENT').[3]

The conditions of the programme are such that patients of 'childbearing potential' should:

- Receive counselling on the risks of valproate and the need for effective contraception.
- Have a signed Annual Risk Acknowledgement Form (ARAF).
- Receive highly effective contraception.
- Have a review with their specialist at least annually.

This guidance intends to outline the roles and responsibilities to support the safe management of patients prescribed valproate as outlined in PREVENT, and to detail the local processes and activities within NCL to minimise the risks associated with initiation and ongoing prescription of valproate (including patient identification, referral, review, clinical coding, prescribing, dispensing, counselling, contraceptive choices, incident reporting and ongoing audit).

5. Patient pathway

To better understand the roles and responsibilities detailed in this guidance, it is important to understand the patient pathway and where each healthcare professional has an active role in minimising the risk of harm to the patient. A best practice patient pathway is demonstrated in **Figure 1**.

6. Roles and Responsibilities

It is the responsibility and duty of all healthcare professionals involved to ensure that patients of childbearing potential do not use valproate unless the Pregnancy Prevention Programme ('PREVENT') is in place. Any use outside of PREVENT is contraindicated and considered off-label. This means that the prescriber assume full responsibility for every prescription of valproate made outside of PREVENT (see MHRA advice for prescribers for off-label or unlicensed use of medicines).

All practitioners who prescribe valproate should be aware of the supportive risk management materials available from the MHRA:

- The PREVENT guide for healthcare professionals
- The PREVENT patient guide
- The valproate patient card
- The Annual Risk Acknowledgement Form (ARAF)

The responsibilities for each step in the patient pathway are described below.

6.1. New initiation of valproate in people of childbearing potential

The specialist intending to initiate valproate will:

- Only initiate valproate if there is a clear indication (current licenced indications include epilepsy and bipolar disorder) & alternatives are ineffective/not tolerated.
- Exclude pregnancy by means of a negative plasma pregnancy test prior to initiation (Note: should be repeated 3 weeks after latest unprotected sexual intercourse).
- Discuss the PREVENT programme with the patient:
    - Inform the patient of the teratogenic risk with valproate to an unborn child if valproate were to be used during pregnancy.
    - Discuss the requirement for highly effective contraception for people of childbearing potential throughout treatment with valproate without interruption.
    - the need for an annual risk review with the specialist, and for additional appointments as soon as the person is planning pregnancy.
    - Inform the patient to contact their GP urgently if pregnancy is suspected.
    - Provide the patient with a copy of the PREVENT patient guide.
- If the person lacks capacity to make an informed decision to consent to treatment with valproate, there should be a best interests discussion around initiating valproate; the details should be recorded in documentation such as the patients electronic notes and ARAF.[4]
    - There should be an additional capacity assessment regarding the need for highly effective contraception (see Section 7.3 for more information).
    - Information on valproate and highly effective contraception should be provided to the patient in a format that they can understand and on the risks with valproate use during pregnancy to their parents/caregiver/responsible person.
- Ensure the patient/caregiver/responsible person understands the need to comply with contraception throughout treatment and undergo pregnancy testing when required.
- Unless competent and confident to discuss contraception with the patient themselves, make a referral to sexual health services (or GP, if commissioned) to discuss contraceptive options with the patient and arrange for administration of a patient-independent method or prescription (see the section on highly effective contraception below).
- Only initiate valproate therapy once highly effective contraception has been confirmed (please see Section 7 for information on how to manage situations where contraception may not be appropriate or cannot be confirmed in patients with childbearing potential).
- Complete and sign a copy of the ARAF (ideally, this is in an electronic format):
    - If the patient is not required to be on PREVENT, Step 1 on the ARAF must be completed with rationale clearly documented; Steps 2 and 3 could be completed (i.e., not mandatory) so the patient is aware of the risks if their situation changes in the future.
    - If PREVENT applies, Step 1 remains blank, but Step 2 and Step 3 must be completed
    - If the patient declines PREVENT, the ARAF is not completed; the specialist will write to the GP to inform them that PREVENT was declined
- If the absence of risk is not permanent (i.e. where pregnancy risk is absent but will return, for example, the patient has not yet reached menarche at the time of initiation), inform the patient/caregiver/responsible person that they do not need to be on PREVENT currently, but MUST be made aware of the need to be enrolled onto PREVENT if the patient's circumstances change; they must alert the specialist if circumstances change before the next annual review.
    - In these circumstances, the specialist will discuss the risks with the patient/caregiver/responsible person and clearly document the discussion and rationale in the electronic patient record and the ARAF (completing the 'step 1' part of the form).

- Upload the ARAF to the local electronic patient record and send a copy via email to the GP (if completed by hand, a copy should be scanned for uploading and email). A copy should also be printed and given to the patient (inform the patient to present their ARAF to the pharmacy upon collection of their first prescription of valproate).

6.2. Contraception

- **Note regarding menopause and perimenopause:** The contraceptive methods described below should be used in patients of childbearing age and needs to continue until menopause is confirmed. Perimenopause is the period of time where a patient could potentially suffer from symptoms of menopause but still has childbearing potential. To avoid misdiagnosis of menopause instead of perimenopause, ensure the patient has been confirmed as having entered menopause before adding the diagnosis and/or SNOMED code to their record. Menopause is confirmed in otherwise healthy women aged ≥45 years if they have not had a period for ≥12 months only if they are not using hormonal contraception (patients using hormonal contraception should discuss options for alternative contraceptive methods from the age of 50 onwards with their GP or sexual health service).
    - The FSRH recommends that if amenorrhoea is experienced in patients between 40-50 years of age, contraception should be continued for a further two years before stopping. If amenorrhoea is experienced in patients >50 years of age, contraception should continue for one year before stopping.
    - The FSRH also recommends that where using a contraceptive method that obscures menopause (e.g., progestogen-only implant, progestogen-only pill or levonorgestrel intrauterine-system), contraception can be stopped at age 55.
    - Further information can be found in the FRSH guidance for contraception in women aged over 40 years (https://www.fsrh.org/standards-and-guidance/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/).
- At least one 'highly effective' method of contraception or two complementary forms of contraception (including a barrier method) should be used in patients of childbearing age.
- **Highly effective contraceptive** options have <1% failure rate. Highly effective contraception is considered to be **user-independent** forms, including:
    - Long-acting reversible contraception (LARC), such as:
        - Intrauterine device (IUD); also known as a copper intrauterine device (Cu-IUD)
        - Levonorgestrel intrauterine system (LNG-IUS)
        - Progestogen-only implant (IMP) - Please note effectiveness of the IMP is reduced if taking any enzyme inducing medicines
    - Female sterilisation
- **Complementary** forms of contraception are **user dependent** methods of contraception have a failure rate >1%. This includes Combined Oral Contraceptives (COC), the Progestogen-Only contraceptive Pill (POP), Depot Medroxyprogesterone Acetate (DMPA) injections and fertility awareness-based methods are not considered highly effective since the typical use incorporates user failure risks. Failure rates with DPMA injections are due to repeat injections being missed or administered late; if there are regular documented administrations, this may be deemed a highly effective form of contraception.
- When choosing a contraceptive method, individual circumstances are evaluated, and the patient should be involved in discussion to ensure engagement and compliance. Even if the patient has amenorrhoea, she must follow all the advice on highly effective contraception.

The specialist intending to initiate or continue valproate will:

- Discuss the requirement for highly effective contraception with the patient.
- Unless competent and confident to discuss contraception with the patient themselves, make a referral to sexual health services (or GP, if commissioned) – see the NCL guidance on referral for contraception for information on how and where to refer patients);

- Only initiate valproate once highly effective contraception has been confirmed with the patient (please see Section 7 for information on how to manage situations where contraception may not be appropriate or cannot be confirmed in patients with childbearing potential)

The commissioned GP/sexual health service specialist will:

- Accept referrals from specialists intending to initiate or continue valproate to arrange a consultation to discuss contraception with the patient.
- Discuss the contraceptive choices available with the patient, and work with them to agree on the most suitable and appropriate choice.
- For children or for patients without the capacity to make an informed decision, discuss contraception with the parents/caregiver/responsible person, and ensure they understand the content.
- Arrange for administration of a user-independent form of contraception if this is the preferred option.
- Write to the referrer to inform of the contraceptive choice and, if a user-independent form is chosen, the date of administration.
    - If the patient opts for an oral contraceptive (COP or POP), ensure the referrer is aware so that they may continue prescriptions.
    - If the patient opts out of contraception, ensure this is clearly communicated to the referrer (note for service provider: it is crucial to inform the referrer as soon as possible as valproate is contraindicated in patients with childbearing potential who do not have effective contraception, and therefore any prescribing is off-label).
- If a fitted LARC is removed and not replaced, ensure this is clearly communicated to the patients GP (and if they are still taking valproate and have childbearing potential, counsel the patient to discuss with their GP). Whilst it is not routine to send communications to the GP for removing and not re-fitting LARC, this is of particular importance when the patient is on a teratogenic drug like valproate.

6.3. Dispensing a prescription in hospital pharmacy

The hospital pharmacist will:

- Ensure newly initiated patients are signed up to the PREVENT programme, by checking:
    - A valid ARAF has recently been completed.
    - That the patient has been counselled on the risks associated with valproate.
    - That if eligible and steps 2 and 3 on the ARAF form are completed, that the patient is on highly effective contraception prior to the initial prescription dispensing (or, if for continuation, a referral has been made for contraceptive review and consultation).
    - That a recent negative pregnancy test has been conducted and is documented in the patient notes prior to signing up to PREVENT.
    - That the patient has a PREVENT patient guide and a valproate patient alert card.
- The hospital pharmacist should document that they have checked for a valid ARAF, the date the form was completed, the pharmacist initials and the screening date.
- In exceptional circumstances, valproate may be initiated off-label in certain scenarios where the patient is not enrolled onto PREVENT (e.g., in patients who lack capacity with learning or physical disability which prevents them from becoming pregnant). In these circumstances, an ARAF will not be furnished. The pharmacist should reassure themselves that this is an appropriate off-label use of valproate.
- Upon screening, the pharmacist should ensure there are no interactions with the chosen method of contraception and current concurrent medications (for more information on interactions with hormonal contraception, see FSRH guidance).
- Valproate should be dispensed in the manufacturers' original pack (as this contains specific warnings and pictograms, including a patient card and patient information leaflet, alerting patients to the risks to unborn babies if used in pregnancy).
    - In exceptional circumstances, an exception to the requirement to dispense in the manufacturers' original pack can be made on an individual patient basis. This should only happen following a risk assessment that refers to the need for different packaging (e.g., in a monitored dosage system, or discharge medication for short-term leave from an inpatient unit). The pharmacist should inform the patient and/or carer why a full pack is not being dispensed and ensure a patient information leaflet is provided.
    - If valproate is being dispensed from the original pack into an unmarked box, it is good practice to add a sticker warning of the teratogenic effects of valproate. This can be obtained from Sanofi medical information department (0845 372 7101 or UK-Medicalinformation@sanofi.com).

6.4. Receipt of documentation and clinical coding in primary care

The appropriate clinician in the practice (e.g., GP, pharmacist, nurse or other appropriately trained clinician) will:

- Upon receiving documentation relating to valproate, PREVENT or contraception (e.g., an ARAF and/or letter from the consultant, or contraceptives being administered in community sexual health services), store it in the patient's electronic record.
- Upon receiving an ARAF, use the "Valproate Pregnancy Prevention Review" template in EMIS (using the "Receipt of ARAF" page) to record the outcome of the ARAF.
    - The EMIS template will automatically apply the appropriate SNOMED codes to the patients record. If for any reason the template cannot be used, please apply the appropriate SNOMED code from the list in Appendix 1).
- If the request valproate is new to the practice, ensure that an associated code for the indication has also been applied to the patient's electronic record.
- If PREVENT is not required due to a clinical reason, please ensure an appropriate code has been applied to the patient's record (e.g., hysterectomy)
- A code should be applied to demonstrate a referral to the specialist has been made for ARAF completion (note: if the NCL referral form is used, this SNOMED code will be applied automatically)
- Other codes may be required depending on patient circumstance. These may include:
    - Whether the patient has a learning disability
    - Whether the patient is pregnant

6.5. Continuing prescriptions in primary care

The primary care prescribing clinician (e.g., pharmacist, GP, nurse) will:

- Upon receipt and accepting of a request to continue valproate prescriptions in primary care, ensure the EMIS template "Valproate Pregnancy Prevention Consultation" has been completed to ensure the appropriate SNOMED codes have been applied; also ensure that a code associated with the diagnosis has been applied (see Section 6.4).
- Prescribe valproate for people of childbearing potential where they can be reassured that it is used within the remit of PREVENT (however, they may also be able to issue prescriptions outside of the remit of PREVENT but that this constitutes an off-label use of the drug for which they are responsible for).
- Operate within the remit of PREVENT, ensuring that:
    - The practice has received a valid ARAF (i.e., completed within the previous year).
    - The patient is using highly effective contraception, if indicated.
    - There is no change to the patients' circumstances since the ARAF was completed that may affect the status of the ARAF (e.g., if the patient has reached menarche)
- Continue prescriptions throughout the valid ARAF period
- Refer patients who have an expired, expiring, or absent ARAF as soon as practicable back to the specialist (if a referral is not already completed) for a review and completion of a new ARAF
    - If a patient has been referred to their specialist, valproate prescriptions can continue but should only cover the period until their review date (note that if the ARAF is expired, this is off-label but in the patients' best interests)
- If pregnancy is suspected, ensure that they:
    - Perform an urgent plasma pregnancy test.
    - Refer the patient back to their specialist urgently for a review within days and make a follow-up call to (see information on referral in Section 6.9)
    - Inform the patient not to stop taking valproate until reviewed by the specialist
- If the patient is planning a pregnancy, make an urgent referral back to the specialist (see Section 6.9)
- Ensure that any new medications initiated for the patient do not interact with their current medications, in particular valproate and contraceptives (for more information on interactions with hormonal contraception, see FSRH guidance).
- GPs should respond to queries from other healthcare professionals in a timely manner where there are concerns regarding an issued prescription. For instance, where a community pharmacist identifies that a patient prescribed valproate may be pregnant.

6.6. Dispensing by the community pharmacy

The community pharmacist will:

- Ensure patients of childbearing potential prescribed valproate are aware of PREVENT and that they are signed up to the PREVENT programme.
    - This can be upon discussion with the patient/caregiver/responsible person (if not in person, then via telephone call), or by checking with the GP, checking for prescription endorsements, system notes or confirming via the local electronic records where appropriate and with patient consent
    - In exceptional circumstances, valproate may be initiated off-label in certain scenarios where the patient is not enrolled onto PREVENT (e.g., in patients who lack capacity with learning or physical disability which prevents them from becoming pregnant). In these circumstances, an ARAF will not be furnished. The pharmacist should reassure themselves that this is an appropriate off-label use of valproate.
- Ensure the patient has a patient guide
- Make a supply of valproate based on the individual patient circumstances:
    - If the pharmacist is reassured of the patient being signed up to PREVENT, a routine supply of valproate is completed.
    - If the pharmacist is not reassured that the patient is signed up to PREVENT or is aware that the patient is planning pregnancy – but there is no immediate risk of pregnancy – refer urgently to the GP for assessment and continue to dispense valproate.
    - If there is suspected pregnancy, refer the patient URGENTLY back to their GP, who can refer onward to the specialist for assessment within days (see Section 6.9); valproate should be continued until the specialist review.
        - The patient should continue to take valproate until their specialist review but may not need to continue taking it thereafter.
        - If the patient has enough valproate to cover a period of at least 2 weeks, arrange with the patient to hold dispensing of the prescription until their review has concluded.
        - If the patient does not have enough valproate and the quantity prescribed is more than 2 weeks supply, consider discussing with the GP to prescribe a suitable quantity to cover the interim period until the review has concluded.
- Valproate should be dispensed in the manufacturers' original pack (as this contains specific warnings and pictograms, including a patient card and patient information leaflet, alerting patients to the risks to unborn babies if used in pregnancy).
    - In exceptional circumstances, an exception to the requirement to dispense in the manufacturers' original pack can be made on an individual patient basis. This should only happen following a risk assessment that refers to the need for different packaging (e.g., in a monitored dosage system, or discharge medication for short-term leave from an inpatient unit). The pharmacist should inform the patient and/or carer why a full pack is not being dispensed and ensure a patient information leaflet is provided.
    - If valproate is being dispensed from the original pack into an unmarked box, it is good practice to add a sticker warning of the teratogenic effects of valproate. This can be obtained from Sanofi medical information department (0845 372 7101 or UK-Medicalinformation@sanofi.com).

6.7. Identifying patients with expiring/expired ARAF

Currently the most appropriate mechanism to identify patients with expiring, expired or absence of a valid ARAF form in NCL is is by using the purpose-built searches in the EMIS system (which can be found under the title “”). ICS regions outside of NCL may use alternative electronic patient record systems, although should follow a similar search strategy (outlined in Appendix 2)

To complement the EMIS searches, a population health dashboard has been produced on the HealtheIntent platform. The dashboard is designed to mirror the EMIS search, but presents the data with infographics, an easy-to-use interface and risk stratification of all patients to outline the necessary course of action (see Appendix 2). Please note that there may be a very small number of patients who have declined to share their data on the dashboard, so all users should perform a periodic validation check for good practice (at least annually) to compare the number of patients determined by an EMIS search against the dashboard for your local practice/PCN).

To use the dashboard, clinicians will need to ensure they are registered. To register, please email nclicb.digitalhelpdesk@nhs.net. A user guide for the valproate dashboard can be found in Appendix 2.

The dashboard can be found via https://nlhcr.analytics.eu.healtheintent.com/. Please note that your access is subject to data protection; if you do not have authorisation from GP practice(s) that you work in, you will not be able to use the case finding tool (though you will be able to view aggregate data on the overview page for NCL).

GP practices will:

- Ensure that a periodic search for patients of childbearing potential prescribed valproate is scheduled at least every six months.
- Ensure they identify which clinician/team will identify patients who require reviews and undertake contraceptive reviews for the practice (as per below).

The appropriate primary care clinician (e.g., primary care pharmacist/technician) will:

- Identify patients of childbearing potential and prescribed valproate via their clinical search system (e.g., EMIS or SystmOne), or by using the purpose-built HealtheIntent dashboard (if this is available and has been validated against an EMIS search in your local practice/PCN)..
- Ensure that they immediately notify the GP and specialist if they identify any patients who are pregnant and being prescribed valproate and follow the appropriate local mechanisms for incident reporting (see Section 6.13).
- Identify patients who do not have a valid ARAF, or have an expiring ARAF:
    - Contact the patient to enquire whether they have been reviewed by their specialist.
    - If the patient is not signed up to PREVENT, consider whether the risk of pregnancy was permanently or temporarily absent. Ask the patient/caregiver/responsible person if their circumstances have changed recently.
        - Patients who have a permanent or temporary absence of pregnancy risk do not need an annual review but do need at least one ARAF (Step 1) completed.
        - If a patient has a permanent absence of pregnancy risk (e.g., post-menopausal women or hysterectomy) and does not have a completed Step 1 on file, contact the relevant specialist (e.g., via ‘Advice & Guidance’) first to discuss before making a referral back; possible resolutions include transmission of an existing ARAF held by the specialist, a virtual consultation, or for a referral to the specialist to review the patient’s condition and current medications.
    - If a specialist review has not been undertaken in the previous year and the patient fits the criteria for PREVENT, inform the patient a referral will be made to see their specialist.
    - Complete an NCL referral form for ARAF review. If referring to their hospital specialist, send via EMIS; if referring to the community mental health team, please email the form (see Appendix 3 for contact details).

- If the patient hasn't had a contraceptive review in the past year:
  - Check the patients electronic record to see if there is any information on a contraceptive review (e.g., letter from a sexual health service, or completion of the EMIS template page for contraceptive review).
  - If there is no evidence of review for adequate contraception, contact the patient and perform a contraceptive review (completing the relevant form within the "Valproate Pregnancy Prevention Consultation" EMIS template).
  - If contraception is not adequate, refer to their GP or local sexual health service.
- If unable to use the EMIS template, apply relevant SNOMED codes (see Appendix 1)

6.8. Audit

Borough medicines management teams/ICB Medicines Safety Officer will:

- Analyse the aggregate level data on the HealtheIntent dashboard for PCNs across their respective Borough annually (starting from 1 year following the publication of this guidance) to determine:
    - The number of patients of childbearing potential in their region prescribed a medicine containing valproate.
        - Percentage of people with childbearing potential prescribed valproate who have a coded PPP entry in their EMIS record
        - Percentage of people with childbearing potential prescribed valproate and enrolled on the PPP who have an ARAF coded within their EMIS record within the last 12 months
- If patients are identified without a valid ARAF or without being enrolled on to PREVENT, contact the relevant PCN pharmacist to identify:
    - The proportion of patients without a valid ARAF that have had a referral made to their specialist versus those who have not.
    - The proportion of patients appropriately excluded from enrolment onto PREVENT versus those who are inappropriately excluded.

Provider Trust Medicines Safety Group will:

- Organise for undertaking and feedback of annual audit:
    - The indication for which valproate is being prescribed:
        - Epilepsy
        - Bipolar disorder
        - Schizophrenia/Schizoaffective disorder
        - Migraine
        - Other (please state)
    - The number of patients of childbearing potential who were reviewed for ARAF completion; of which:
        - Number of patients/caregivers who were enrolled onto PREVENT
        - Number of patients/caregivers who did not require to be enrolled on to PREVENT (i.e., temporary or permanent absence of pregnancy risk)
        - Number of patients/caregivers who refused to be on PREVENT
    - If PREVENT is refused/non-compliant:
        - Was valproate continued (off-label)?
        - If valproate was not continued:
            - was valproate switched to an alternative medicine? (If so, please state which)
            - After attaining a stabilised dose, did the condition or symptoms (e.g., seizure frequency and intensity, symptom severity etc) worsen, improve, or stabilise?

6.9. Which patients should be referred to their specialist for annual ARAF completion

Patients that should be referred to their specialist annually:

- Patients aged 0-60 who have the potential to become pregnant.

Patients that are excluded from an annual risk assessment with their specialist:

- Patients with a permanent absence of pregnancy risk
    - If the person is newly initiated on sodium valproate, they will have a Step 1 ARAF completed and sent to their GP for continued prescribing. No further annual risk assessments are necessary. Although the MHRA ARAF has a 1-year expiry, an ARAF that states the absence of pregnancy risk is permanent (e.g., due to menopause) is only required once in the patient's lifetime.
    - If the patient has a permanent absence of pregnancy risk (i.e., there is no risk that the patient can physically become pregnant, such as post-menopause) and has been prescribed valproate from their GP but has never had a Step 1 ARAF completed, then a referral to their specialist is not required (as there is no pregnancy risk). Ensure the correct SNOMED code for their permanent absence of pregnancy risk has been applied to the patients record.
- Patients with a temporary absence of pregnancy risk who have a Step 1 ARAF on file AND confirmation that the rationale for temporary absence of pregnancy risk is still present (e.g. patients who are pre-menarche).
- Patients who have childbearing potential but BOTH Specialist and GP are in agreement that circumstances preclude them from becoming pregnant (e.g., patients with a learning disability who lack the capacity to consent), and annual referrals for ARAFs would otherwise be distressing (note: if these circumstances change in the future, it is reasonable to consider discussion and/or referral to the specialist).
    - See Section 7.3 for more information.

6.10. Referral of existing patients on valproate to the specialist service

The primary care clinician (GP/ PCN or practice pharmacist/ community pharmacist/ nurse) will:

- Refer eligible patients of childbearing potential prescribed valproate for an annual assessment with their specialist:
    - If the referral is being made on EMIS (using the "valproate risk assessment referral form") via ERS, this can be routinely performed using the NCL referral form for an ARAF review
    - If this is being made from a premises without EMIS, this can be done by e-mailing the relevant clinic (please see the list of specialist centre clinics in Appendix 3). Any non-EMIS referrals needs to contain:
        - Patient details (name, address, contact details, registered GP practice details and NHS/hospital number if known)
        - Whether the patient can understand English (or otherwise their first language)
        - Whether the patient has a severe mental illness, learning disability or physical disability
        - Details of the care giver or responsible person, if applicable
        - Past medical history
        - Drug history
        - Allergies
        - Valproate indication and dose
        - Current specialist
        - Whether contraception is required (or if not, please state the reason)
        - If required, is contraception in use currently? Please provide details of the contraceptive (in the case of long-acting contraception, when it was administered if known)
        - Whether an ARAF has been completed and is valid
- If the referral is being made for a patient who is planning a pregnancy or is pregnant, please ensure the referral is marked as 'URGENT' (ensuring it contains direct contact numbers) and call the clinic to inform that the referral has been sent through to ensure receipt.
- If the referral is being made by community clinicians with no direct communication lines back to the specialist possible, and there is risk of pregnancy, refer urgently back to the GP for initial assessment.
- For clinical teams outside of NCL: Please note, if you are referring a patient from out of area to an NCL specialist, there is an expectation that you adhere to the NCL formulary. Valproate medicines do not require a shared care protocol for transfer of prescribing responsibility in NCL.

6.11. Specialist review of adult patients established on valproate

The specialist intending to continue valproate will:

- Accept primary care referrals for people of childbearing potential on valproate (including emergency referrals in the case of unplanned pregnancy, or urgent referrals in the case of planning a pregnancy).
    - If the referral is urgent, the primary care clinicians will mark it as urgent and call the specialist clinic to inform of the referral made; the specialist team should do their upmost to prioritise these referrals for urgent consultations as soon as practicable.
- Decide with the patient whether they are to continue taking valproate
    - Treatment is only continued if other treatments are ineffective or not tolerated, and there are no imminent plans for the patient to become pregnant
- Discuss and reaffirm the need to be on the PREVENT programme with the patient.
- Complete an ARAF form, ensuring the patient is counselled as you would for new initiations of valproate and provide a PREVENT patient guide if misplaced (see Section 6.1 for details on patient counselling and storing/sending the ARAF).
- Refer to contraception services for follow-up if needed (though note whether the referrer has indicated if the patient has already been referred or has active contraception)
- If a patient declines to be on the PREVENT program, this should be communicated to the GP in writing. The GP should be informed whether it is the patient, parent or caregiver who has declined, and that any further prescribing is off-label
- Where possible and electronic systems allow, book a patient in for their next annual review in 12 months' time. If this is achieved, inform the GP practice of the patients next appointment date.

6.12. Review of paediatric patients who have recently entered menarche

The specialist will:

- Accept referrals for patients currently receiving valproate who have entered menarche (or otherwise annually).
- Only continue valproate if there is a clear indication and other treatments are ineffective or not tolerated.
- If valproate is to be continued, highlight the risks to an unborn child from treatment with valproate in pregnancy and the need for the patient to be enrolled on the PREVENT programme upon menstruation.
- Provide information and advice on highly effective methods of contraception and on the use of valproate during pregnancy to their parents/caregiver/responsible person and make sure they clearly understand the content (or if not confident or competent, to refer to sexual health services to discuss contraception)
- Review and counsel the patient as per Section 6.1:
    - Note that previous ARAFs will have indicated in step 1 that the patient had not reached menarche; this will no longer be applicable, and a new ARAF will need to be completed.
    - Complete and store/send the ARAF as per Section 6.1.
- In the case of transfer from paediatric to adult services, the referring paediatric consultant should communicate all relevant information relating to on-going treatment with valproate in people of childbearing potential, including:
    - The risk versus benefit assessment of on-going treatment with valproate.
    - Discussions with the patient or their carer about treatment with valproate, including the need to use effective contraception.

6.13. Specialist review of patients who are pregnant or planning pregnancy

The hospital specialist will:

- Review patients who present with an unplanned pregnancy to consider switching to another treatment if appropriate.
    - For more information on safety of antiepileptic drugs during pregnancy, see the MHRA review
    - Use of valproate medicines in patients who are pregnant are off-label use and outside the scope of this guidance; any considerations of use should be via local Drugs and Therapeutics Committee.
- Review patients who are planning pregnancy:
    - Ensure the patient understands the risks associated with taking valproate in pregnancy.
    - Switch to another therapeutic option which is suitable in pregnancy, if appropriate (for more information on safety of antiepileptic drugs during pregnancy, see the MHRA review)
    - Advise not to stop contraception until the switch is achieved and the patient is no longer taking valproate
    - Continuation of valproate medicines in patients who are planning pregnancy without switching is outside the scope of this guidance; any considerations of use should be via local DTC.

6.14. Incident reporting

- If a patient is identified to have used valproate whilst being pregnant, a local incident report form (e.g., DATIX) and, ideally, a root cause analysis, should be completed.
- Please follow local guidance for incident reporting
- The healthcare professional identifying the error should ensure that the patients GP practice, specialist, and pharmacy are made aware of the error to ensure they also follow their local guidance for incident reporting

7. Considerations for common scenarios

7.1. Patients that do not engage with services or PREVENT

- According to the product licence, valproate is contraindicated in patients of childbearing potential unless conditions of PREVENT are met (which includes the need to have regular reviews and demonstrate understanding of the risks from taking valproate in pregnancy).
- The decision of whether to continue off-label valproate in patients who do not want to engage with services, or those who attend but do not wish to comply with the criteria within PREVENT, must be balanced carefully with the individual circumstances of the patient.
- The benefits and risks must be carefully considered, and where appropriate discussed in an MDT setting. Where valproate is contraindicated, discontinuing treatment may prevent avoidable harm from potential pregnancy in the future. However, stopping treatment could cause the patients' condition to worsen; this is particularly concerning in patients with highly-refractory epilepsy or those at risk of sudden unexpected death in epilepsy (SUDEP).
- Patients who choose not to engage with services may do so due to fears that valproate will be stopped or switched without their input. Where concerns arise, patients should be reassured that their thoughts and opinions are pivotal to their management plan.

7.1.1. If a patient does not attend appointments with the specialist:

- The specialist should inform the GP and offer the patient another appointment
- If the patient does not attend several appointments, the specialist should contact GP and to discuss how best to proceed for the individual patient.

7.1.2. If a patient does not attend GP appointments:

- Primary care teams should make attempts to contact the patient to offer another appointment.
- If the patient does not attend several appointments, primary care teams should liaise with the patients' specialist for advice.
- The GP and specialist should discuss how best to proceed with the individual patient. If the patient has an immediate need for valproate, and there is no risk at present (i.e., the patient is not pregnant), prescriptions for a limited duration of valproate should continue until a joint discussion with the specialist has taken place.

7.1.3. Following joint discussions between the specialist and GP:

- Where a specialist and GP make a joint decision that continuing valproate is in the best interest of the patient, this should be clearly documented in both the Trust and Primary care electronic patient record, including rationale
- Where a specialist and GP make a joint decision that discontinuation of valproate is in the best interest of the patient, clinicians should make every effort to contact the patient to discuss an ongoing management plan

7.2. Patients that engage but do not wish to sign up to PREVENT

- If a patient is engaging but does not wish to sign up to PREVENT (e.g., due to personal beliefs such as cultural or religious reasons, or because they do not wish to use contraception owing to possible adverse effects), then the responsible clinician should follow GMC advise on shared decision making with the patient. This includes the following[5]:
    - Information shared should be objective. Share information about reasonable alternatives. Do not apply pressure on the patient to accept your advice.
    - Explore what risks a patient would and would not be prepared to take, and how the likelihood of a particular outcome might influence their choice

- Provide clear, accurate and up-to-date information, based on the best available evidence, about the potential benefits and risks of harm of the options available
- Use visual or other explanatory aids to support patients to understand their personalised risk
- Support patients to understand and retain relevant information & use it to reach a decision
- Check the patients understanding of relevant information and their expectations about the likely outcome of each option
- Respect a patient's right to decide

- Where there is still concern, the responsible clinician should discuss with the GP/specialist to decide the best course of action, and the overall benefit/risk ratio (as per above).

7.3. Patients with severe physical and/or intellectual disability

- In patients who have childbearing potential but suffer from severe physical and/or intellectual disability, sexual intercourse may be unlikely. In these circumstances, it may be distressing for patients and their families to require regular reviews to discuss pregnancy risk and contraception. Therefore, it may be appropriate for prescribing to continue in general practice without the completion of annual risk acknowledgement forms or for the patient to be on 'PREVENT'.
- Clinicians must bear in mind that prescribing valproate in **any** patient with childbearing potential without adequate contraception and a valid ARAF remains off-label prescribing practice.
- If primary care physicians accept off-label prescribing responsibility, **please ensure you apply the SNOMED code** 1129791000000104 (stating the patient does not need to be on PREVENT). This can be entered using the EMIS template or by applying the SNOMED code manually.
- **Patients who have childbearing potential that lack mental capacity**
  - **If newly initiated**, the specialist should evaluate the patient and decide, after discussion with the patient/caregiver, if there is a risk of pregnancy. Where the specialist deems there to be no risk of pregnancy, Step 1 of the ARAF should be completed to highlight the permanent absence of pregnancy risk, and this should also be clearly documented in any notes and correspondence with an indefinite date of expiry. This should be discussed with the GP prior to transfer (as the GP will be asked to undertake off-label prescribing). If in agreement, the primary care team should ensure they apply the SNOMED code stating the patient does not need to be on PREVENT as described above.
  - If the patient has been under the care of the GP for valproate and has never had a Step 1 ARAF completed, the GP should acknowledge that prescribing valproate for this patient is off-label. There are several options available to the GP, who may:
    i. Depending on the scenario, be sufficiently reassured of the absence of pregnancy risk and continue prescribing valproate off-label (applying the SNOMED code as described above); **or**
    ii. Discuss with the patients' Specialist via Advice & Guidance (without referral back) and if both agree, can continue prescribing valproate off-label (applying the SNOMED code as described above); **or**
    iii. Refer the patient back to their specialist to complete a Step 1 ARAF to keep on the patients record and apply the SNOMED code as described above (GPs should continue to prescribe valproate whilst awaiting the form to be completed).
- **Patients who have childbearing potential with severe intellectual or physical disability and have mental capacity**
  - The patient should be involved in discussion. There should be careful evaluation over whether there is an absence of pregnancy risk, and whether the patient has capacity to consent to receive contraception as well as valproate. Although patients with capacity

have the right to be sexually active, the specialist should be alert to the possibility of sexual abuse. The specialist may wish to involve others (e.g., best interest meetings, adult safeguarding, sexual health services etc).

- Any use of valproate in a patient where the patient is not enrolled on to PREVENT should be discussed with the primary care physician before considering transfer of prescribing responsibility due to the potential off-label nature. Please apply the SNOMED code as above.

7.4. In the treatment of status epilepticus

- In certain clinical situations, valproate may the most appropriate option for the emergency treatment of uncontrolled seizures or status epilepticus.
- Clinicians may need to make rapid assessments and best-interests' decision in the acute setting; an urgent pregnancy test may be considered but should not delay treatment of this life-threatening emergency. Any use of valproate in these situations should be documented along with clinical rationale.
- If valproate is to be continued once the patient has stabilised, the patient should be informed of the treatment received and consented on to PREVENT.

7.5. Starting or restarting valproate in patients of childbearing potential in the Psychiatric ICU

- Valproate is sometimes initiated in the Psychiatric ICU (PICU) for conditions such as bipolar affective disorder.
- Unless clear evidence of exception (e.g., post-menopausal with a reliable history of no periods for 2 or more years AND a negative pregnancy test), consider women under 50 to have childbearing potential; women aged 50 to 60 years old may have a lower risk of pregnancy, and therefore a single negative pregnancy test will suffice to confirm an acceptably low risk of pregnancy.
- Patients should be counselled on the risks in pregnancy and enrolled on to PREVENT wherever possible. If enrolment onto PREVENT is not possible/refused, consider valproate if there is a clearly documented clinical indication and all other treatments have been ineffective or are not available.
- Valproate should be reviewed routinely; the patients' capacity for enrolment on to PREVENT should also be routinely reviewed if there is consideration for long term prescribing.
- Prior to stepping down/being discharged, the patient should either have a plan to reduce and stop valproate, or there should be a shared agreement between the PICU specialist and the clinician on the accepting ward.
- If transferred, the patient should be subject to routine review; patients should not be routinely discharged on valproate without being enrolled onto PREVENT/without a plan in place for ongoing prescribing of valproate.

7.6. Patients initiated on valproate from a private provider (including clinicians registered abroad)

- There is an expectation that medication initiated by private providers are only taken on by primary care prescribers once they are satisfied that prescribing is appropriate, responsible and what we be considered for NHS patients for equitable treatment.
- Medications suggested by a private provider which are not aligned with national or local guidance will not be routinely continued by the primary care prescriber; therefore, the private provider should only transfer prescribing if they are able to fulfil all the duties of the 'specialist' in this guidance, including acceptance of referrals for the completion of an ARAF

7.7. Patients who withdraw from/have a change in circumstances since enrolment on the pregnancy prevention programme

- Patients may wish to withdraw from the pregnancy prevention programme, or have a change in circumstances (i.e., new hysterectomy) since starting on PREVENT
- The primary care clinician should apply the SNOMED code to demonstrate that the patient has discontinued PREVENT (1129841000000102) and inform the patient's specialist of the change in circumstances

8. References

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3. Medicines and Healthcare product Regulatory Agency. Valproate medicines (Epilim▼, Depakote▼): contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met. GOV.UK. Published April 24, 2018. Accessed September 29, 2020. https://www.gov.uk/drug-safety-update/valproate-medicines-epilim-depakote-contraindicated-in-women-and-girls-of-childbearing-potential-unless-conditions-of-pregnancy-prevention-programme-are-met

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5. Shakespeare J, Sisodiya SM. Guidance Document on Valproate Use in Women and Girls of Childbearing Years. https://www.rcpch.ac.uk/sites/default/files/2021-01/Pan_College_Guidance_Document_on_Valproate_Use%20V2.1.pdf

9. Associated documents and websites

- MHRA guidance on valproate use by women and girls
- Supportive materials produced by MHRA:
    - The PREVENT guide for healthcare professionals
    - The PREVENT patient guide
    - The valproate patient card
    - The Annual Risk Acknowledgement Form (ARAF)
- MHRA guidance for contraception during treatment with medicines of teratogenic potential
- MHRA review of the safety of antiepileptic drug use during pregnancy
- Faculty of Sexual & Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists guidance on drug interactions with hormonal contraception
- NCL referral information for emergency intrauterine device or long-acting reversible contraception – a document with the relevant contact information for referral into sexual health services, and a complete list of commissioned GP practices who can administer long-acting reversible contraception in NCL
- Contraceptive choices – A website designed to help patients understand the different contraceptive options available to them.
    - The website features a comparison table of all contraceptive options, with the most effective at the top ('highly effective' options are the first 3 rows)
- Patient consultation video – with thanks to the CNWL pharmacy team for producing the video

Appendix 1: SNOMED codes used for clinical coding

Field name	Scenario	Codes name	SNOMED code
Annual Risk Acknowledgement Form (ARAF)	ARAF has been completed (needs to be entered for every patient with a new ARAF, regardless of whether patient is on PREVENT or not)	Annual Risk Acknowledgement Form completed (situation)	1366401000000107
Pregnancy Prevention Programme (PPP)	ARAF indicates that the patient is enrolled on PREVENT	Pregnancy prevention programme started (situation)	1129771000000103
	ARAF indicates that the patient does not need to be on PREVENT	Pregnancy prevention programme not needed (situation)	1129791000000104
	ARAF indicates that the patient declined to be on PREVENT (therefore valproate is contraindicated)	Pregnancy prevention programme declined (situation)	1129801000000100
	ARAF indicates that the patient's parent has declined enrolment on PREVENT (therefore valproate is contraindicated)	Pregnancy prevention programme declined by parent (situation)	1129821000000109
	ARAF indicates that the patient's caregiver has declined enrolment on PREVENT (therefore valproate is contraindicated)	Pregnancy prevention programme declined by caregiver (situation)	1129811000000103
	Patient was enrolled on PREVENT, but their circumstances have now changed (e.g., new hysterectomy, withdrawing due to change of mind) and are no longer on PREVENT	Pregnancy prevention programme discontinued (situation)	1129841000000102
Referral to secondary care for completion of Valproate ARAF	Code used when a referral to a specialist has been completed (note: if the NCL referral form is used, this code is added automatically)	Referral for completion of Valproate Annual Risk Acknowledgement Form (procedure)	1366381000000107
Rationale for the absence of the risk of pregnancy	Codes used for hysterectomy (see individual codes for the most appropriate to the patient's clinical situation)	History of hysterectomy (situation)	161800001
		History of abdominal hysterectomy (situation)	473173007
		History of hysterectomy for benign disease (situation)	428804004
		History of myomectomy (situation)	275574006
		History of postpartum excision of uterus (situation)	860646004
		History of supracervical hysterectomy (situation)	698448004
		History of total hysterectomy (situation)	428078001
		History of radical hysterectomy (situation)	429290001
		History of total hysterectomy with bilateral salpingo-oophorectomy (situation)	429763009
		History of total hysterectomy without abnormal cervical Papanicolaou smear (situation)	10738891000119107
		History of vaginal hysterectomy (situation)	473171009
	Code used for cervical conization	History of cervical conization (situation)	108941000119102
	Codes used for menopause (see individual codes for the most appropriate to the patient's clinical situation)	Menopause present (finding)	289903006
		Premature menopause (finding)	373717006

Field name	Scenario	Codes name	SNOMED code
Learning disability	Codes used to indicate a learning disability (see individual codes for the most appropriate to the patient's clinical situation)	Developmental academic disorder	1855002
		On learning disability register	416075005
		Severe learning disability	508171000000105
		Specific learning disability	889211000000104
		Significant learning disability	931001000000105
		Mild learning disability	984661000000105
		Moderate learning disability	984671000000103
		Profound learning disability	984681000000101
Pregnancy	Codes used to indicate pregnancy (see individual codes for the most appropriate to the patient's clinical situation)	IUD failure - pregnant	169488004
		Pregnant, diaphragm failure	169501005
		Pregnant, sheath failure	169508004
		Pregnant - urine test confirms	169560008
		Pregnant - blood test confirms	169561007
		Pregnant - V.E. confirms	169562000
		Pregnant - on history	169563005
		Pregnant - on abdominal palpation	169564004
		Pregnant - planned	169565003
		Pregnant - unplanned - wanted	169566002
		Pregnant	77386006

Appendix 2: HealtheIntent valproate dashboard user guide

This user guide provides additional information regarding the valproate dashboard, highlighting features, functionality and limitations of this digital tool. This tool has been created using North London Health and Care Records data.

Background to safety and risks of valproate

Valproate is a collective term for medicines including sodium valproate, valproic acid and semi-sodium valproate. Valproate is a medication used to treat all forms of epilepsy, mental health disorders (including bipolar disorder and depression), migraine prophylaxis and pain management. Valproate is associated with a significant risk of physical birth defects (10%) and neurodevelopmental disorders (30-40%) in children born when valproate was taken during pregnancy.

Since 2018, valproate has been contraindicated in people of childbearing potential unless they meet the conditions of a Pregnancy Prevention Programme (PPP, also known as 'PREVENT').

The conditions of the programme are such that patients of 'childbearing potential' should:

- Receive counselling on the risks of valproate and the need for effective contraception.
- Have a signed Annual Risk Acknowledgement Form (ARAF).
- Receive 'highly effective' contraception.
- Have a review with their specialist at least annually.

People of childbearing potential prescribed valproate without a valid ARAF or other mitigating factors (which exclude the risk of pregnancy) , should be referred urgently to their specialist.

The dashboard has two parts:

1. Dashboard overview – *a population snapshot*
2. Case-finding tool – *identifies and stratifies patients for review*

Both parts of the dashboard use the same search criteria to identify patients of childbearing potential:

- Prescribed valproate within the past six months from their NCL GP;
- Aged 0 – 60 years old;
- With sex recorded as female, other, unknown or unspecified

Relevant links (see the NCL valproate guideline for more links)

- ***MHRA guidance on valproate use by women and girls***
- ***NCL valproate risk minimisation guideline***
- ***The PREVENT guide for healthcare professionals***

Valproate case-finding tool

The case-finding tool is aimed at providing clinicians with a record-level list of patients of childbearing potential prescribed valproate in primary care within the last six months. In addition, the case-finding tool provides additional information regarding each patient, including:

- The patient's PPP status;
- Whether an ARAF has been completed within the last 12 months;
- Whether a referral has been made to the specialist for review and completion of the ARAF;
- The patient's risk of pregnancy;
- The speciality area that valproate may have been prescribed for;
- Relevant additional findings;
- And a recommendation regarding the action required for that patient.

In addition, the case-finding tool may be filtered based on four criteria: Organisation, PPP status, speciality area and recommended action.

While the dashboard may make a recommendation and rank patients based on urgency for review, the dashboard has not been designed or validated to replace clinical decision-making.

Further information regarding the stratification can be found in *table 1*, while additional information regarding several fields within the case-finding tool can be found in *table 2*.

Table 1: *Action and Order*

Action	Definition	Criteria	Order
Review or refer	These patients are at highest risk and should be prioritised for review	• Pregnant; and • Aged 0 – 60 years old	1
		• No PPP entry or valid ARAF; • Has LD diagnosis; and • Aged 7 – 60 years old	2
		• No PPP entry or valid ARAF; • Aged 13 – 60 years old	3
		• No PPP entry or valid ARAF; • Aged 7 – 12 years old	4
Keep under review	These patients are not enrolled on the PPP. Whilst there may be good reason for this, these patients may still have a risk of pregnancy. Keep these patients under review. If a permanent absence of pregnancy risk exists (e.g., confirmed menopause), ensure the appropriate SNOMED code has been applied to their patient record.	• PPP discontinued; • PPP not needed; • PPP declined; • PPP declined by parent or • PPP declined by caregiver	5
Consider expiry of ARAF	These patients have a valid ARAF and are enrolled on the PPP. Consider checking if their ARAF is due for expiry soon. Due to capacity at Specialist Trusts, consider making the referral 3-6 months in advance of ARAF expiry.	• Enrolled on PPP and has valid ARAF; • Has LD diagnosis; and • Aged 7 – 60 years old	6
		• Enrolled on PPP and has valid ARAF; • Aged 7 – 12 years old	7
		• Enrolled on PPP and has valid ARAF; • Aged 13 – 60 years old	8
No action required	These patients have a permanent absence of pregnancy risk and therefore no further action is required. It is good practice to ensure the SNOMED codes have been applied correctly.	• Has history of menopause; • Hysterectomy; • Bilateral Salpingo Oophorectomy; • Bilateral Oophorectomy or • Aged 0 – 6 years old	9

LD = Learning disability, PPP = Pregnancy Prevention Programme, ARAF = Annual Risk Acknowledgment Form

Table 2: *Case-finding tool fields, definitions and SNOMED codes searched for*

Field/search criteria	Definition
Cohort search criteria	People recorded as "Females", "gender unknown", "gender unspecified" or "other" aged 0 – 60 years old prescribed sodium valproate or valproic acid from their NCL GP within the last six months.
Pregnancy Prevention Programme (PPP)	This field searches for six codes for the PPP and will display the latest code as "Yes – enrolled", "No - discontinued", "No - not needed", "No - declined", or "No entry found": • Pregnancy prevention programme started (situation) • Pregnancy prevention programme discontinued (situation) • Pregnancy prevention programme not needed (situation) • Pregnancy prevention programme declined (situation) • Pregnancy prevention programme declined by parent (situation) • Pregnancy prevention programme declined by caregiver (situation)
Annual Risk Acknowledgement Form (ARAF)	This field searches for one code within the past twelve months: • Annual Risk Acknowledgement Form completed (situation)
Referral sent to secondary care for completion of ARAF	This field searches for one code within the past six months • Referral for completion of Valproate Annual Risk Acknowledgement Form (procedure)
Risk of pregnancy	**Low risk:** • Zero to six years old, history of menopause, hysterectomy, Bilateral Salpingo Oophorectomy or Bilateral Oophorectomy. **Medium risk:** • Seven to twelve-year-olds **High risk:** • Thirteen years or older without mitigating pregnancy risk factors (see low risk).
Speciality	This field searches for several codes related to both conditions, including bipolar and epilepsy, as well as codes for neurology and psychiatry clinic attendance within the patient's lifetime. Pain and migraine were omitted. At the time of approval, only 4.7% of patients did not have a speciality recorded.
Additional findings	This field searches for: • Pregnancy findings observed within the last nine months • Learning disability diagnosis within the patient's lifetime
Action	• See Table 1.

Limitations of the dashboard and case-finding tool

- The criteria used within the case-finding search has been designed to ensure that people of childbearing potential are not missed if their sex is recorded as unknown, unspecified or other. This may result in people of non-childbearing potential being included in the case-finding tool.
- The dashboard currently cannot pick up patients who have been prescribed valproate from clinicians outside of NCL GPs. Therefore, patients issued valproate by private clinicians or secondary care clinicians will not appear within this search.
    - Due to current data flows within HEI, new patients initiated on valproate by their secondary care specialist will not appear on the case-finding tool until their NCL GP has issued a prescription.
- There is a three to four-day lag between a code being entered in EMIS and the entry appearing within HEI.
- The dashboard will not include people who have opted out of HEI. Therefore, while every effort has been made to ensure that all patients pull through into the dashboard, this cannot be guaranteed.
- There are some known circumstances where false positive pregnancy flags may appear within the case-finding tool due to an “unplanned pregnancy” code used within an ARDENs template. The code remains within the search as the risk associated with not including it was greater than the benefit of its removal.

Appendix 3: Specialist contact details

National Hospital for Neurology and Neurosurgery

Hospital switchboard:	020 3456 7890
Referrals	Via eRs
Advice	Use Advice and Guidance via eRs
Epilepsy nurse helpline (for current UCLH patients only)	uclh.epilepsy@nhs.net Tel: 020 3448 8627
Patient contact:	020 3448 8625 020 3448 8619 020 3448 8609 020 3448 8623

Royal Free London neurology services

Hospital switchboard:	020 3758 2000
Referrals	Via eRs
Advice	Use Advice and Guidance via eRs
Epilepsy nurse helpline	020 7830 2864 rf.epilepsyteam@nhs.net
Patient contact:	Please contact the relevant consultant secretary via the RFL hospital switchboard (as above)

Practice based mental health services

Camden mental health team	Camden.mhct@candi.nhs.uk
Islington mental health team	Islington.mhct@candi.nhs.uk
Barnet mental health team	Complete the "*Mental Health Referral for Adults - Barnet – BEHMHT"* form and send to beh-tr.barnetmhreferrals@nhs.net. To discuss a non-urgent referral: beh-tr.barnetmhreferralsadmin@nhs.net or Tel: 020 8702 4382
Enfield mental health team	For practices with a link worker, referrals go via beh-tr.enfieldpclw@nhs.net or Tel: 020 8702 5530. For practices without a link worker, referrals go via the Enfield Assessment Service: assessmentservice.enfield@nhs.net or Tel: 0208 702 3329.
Haringey mental health team	Adults: Central Core team: beh-tr.central.haringey@nhs.net Tel: 020 8702 6210 West Core team: beh-tr.west.haringey@nhs.net Tel: 020 8702 5111 East Core team: beh-tr.east.haringey@nhs.net Tel: 020 8702 5111 Paediatrics: CAMHS Haringey: beh-tr.camhsreferral@nhs.net Tel: 0208 702 3400

Document control

Date	Version	Amendments
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Groups / Individuals who have overseen the development of this guidance:	NCL Valproate Risk Minimisation Working Group
Groups which were consulted and have given approval:	NCL Specialists, Formulary Pharmacists and Commissioners NCL Medicines Optimisation Committee NCL Joint Formulary Committee
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