NHS
North East London

Valproate Safety Update

The webinar will start shortly.
In the meantime, please note the following:

- The webinar is being recorded
- Slides and the recording will be circulated after the webinar
- Please mute your microphone
- Ask any questions using the chat or Q&A function

NEL Teratogenic Medicines Safety Improvement Group (TMSIG)

April 2025

Agenda

Time	Item	Speakers
1.00 – 1.05pm	Introduction	**Dr Roberto Tamsanguan,** NEL TMSIG Chair, Clinical Director for Tower Hamlets, GP Partner, Tower Hamlets Together & NHS NEL
1.05 – 1.15pm	Safety update	**Natasha Callender**, Head of Medicines Optimisation (Safety, Quality and Governance), Medication Safety Officer, NHS NEL
1.15 – 1.25pm	Dashboard	**Geoff Ingram,** Senior Project Manager, NHS NEL **Sunitha Tanikell**, Senior Developer, NHS NEL
1.25 – 1.35pm	Resources	**Natasha Callender**, Head of Medicines Optimisation (Safety, Quality and Governance), Medication Safety Officer, NHS NEL
1.35 – 1.45pm	Patient case	**Dr Roberto Tamsanguan,** NEL TMSIG Chair, Clinical Director for Tower Hamlets, GP Partner, Tower Hamlets Together & NHS NEL
1.45 – 1.50pm	Actions for primary care	**Dr Roberto Tamsanguan,** NEL TMSIG Chair, Clinical Director for Tower Hamlets, GP Partner, Tower Hamlets Together & NHS NEL
1.50 – 2.00pm	Q&A	All

Learning Outcomes

By the end of the webinar, participants will be able to:

- Describe the current risks and measures to mitigate risks associated with valproate use in girls and women of childbearing potential and boys and men of reproductive potential.
- Understand the updated safety measures when reviewing patients prescribed valproate including risk acknowledgment, PREVENT (pregnancy prevention programme), referral pathways and tools to support communication with patients.
- Use resources shared to assess working practices locally to support safer valproate prescribing.

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Valproate safety update

Background

2015

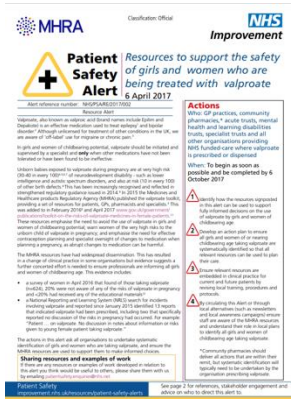
MHRA Drug Safety Update Medicines related to valproate: risk of abnormal pregnancy outcomes

2016

MHRA Drug Safety Update Valproate and risk of abnormal pregnancy outcomes: new communication materials

2017

Patient safety Alert (PSA), NHS/PSA/RE/2017/002 Resources to support the safety of girls and women being treated with valproate.



2018

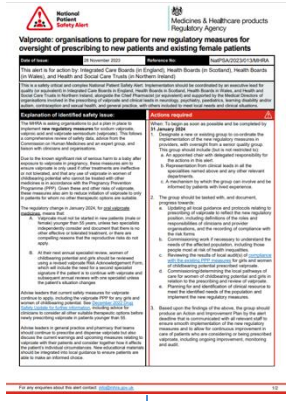
prevent valproate pregnancy prevention programme

MHRA Drug Safety Update Valproate contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme (PPP) are met

2021

MHRA major safety review Antiepileptic drugs: review of safety of use during pregnancy

2023



National Patient Safety Alert (NatPSA) Valproate: organisations to prepare for new regulatory measures for oversight of prescribing to new patients and existing female patients (NatPSA/2023/013/MHRA)

2024

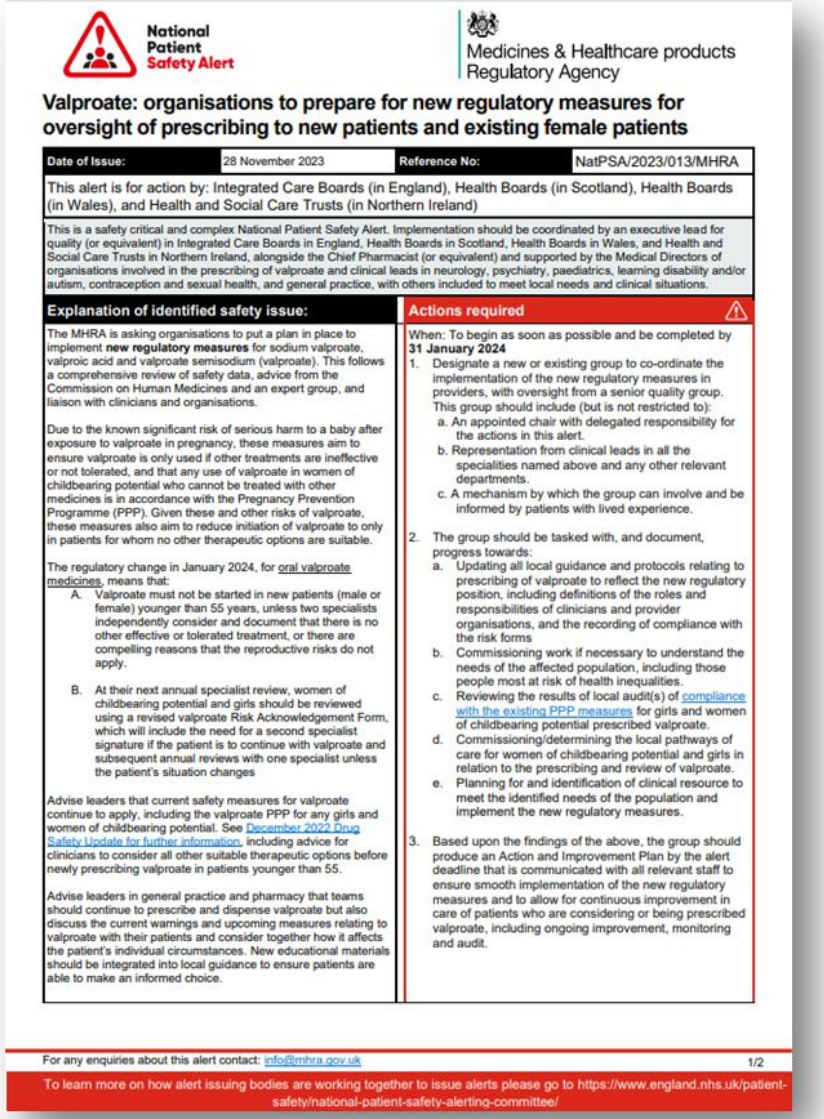
MHRA Drug Safety Update Valproate use in men: as a precaution, men and their partners should use effective contraception

2025

MHRA Drug Safety Update Valproate: review by two specialists is required for initiating valproate but not for male patients already taking valproate

Valproate safety measures

- The regulatory change in **January 2024**, for oral valproate medicines, meant that:
- **Valproate must not be started in new patients** (male or female) younger than 55 years, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.
- At their next annual specialist review, women and girls of childbearing potential should be reviewed using a revised valproate Annual Risk Acknowledgement Form (ARAF), which will include the need for a second specialist signature if the patient is to continue with valproate and subsequent annual reviews with one specialist unless the patient's situation changes.



National Patient Safety Alert

Medicines & Healthcare products Regulatory Agency

Valproate: organisations to prepare for new regulatory measures for oversight of prescribing to new patients and existing female patients

Date of Issue:	28 November 2023	Reference No:	NatPSA/2023/013/MHRA

This alert is for action by: Integrated Care Boards (in England), Health Boards (in Scotland), Health Boards (in Wales), and Health and Social Care Trusts (in Northern Ireland)

This is a safety critical and complex National Patient Safety Alert. Implementation should be coordinated by an executive lead for quality (or equivalent) in Integrated Care Boards in England, Health Boards in Scotland, Health Boards in Wales, and Health and Social Care Trusts in Northern Ireland, alongside the Chief Pharmacist (or equivalent) and supported by the Medical Directors of organisations involved in the prescribing of valproate and clinical leads in neurology, psychiatry, paediatrics, learning disability and/or autism, contraception and sexual health, and general practice, with others included to meet local needs and clinical situations.

Explanation of identified safety issue:

The MHRA is asking organisations to put a plan in place to implement **new regulatory measures** for sodium valproate, valproic acid and valproate semisodium (valproate). This follows a comprehensive review of safety data, advice from the Commission on Human Medicines and an expert group, and liaison with clinicians and organisations.

Due to the known significant risk of serious harm to a baby after exposure to valproate in pregnancy, these measures aim to ensure valproate is only used if other treatments are ineffective or not tolerated, and that any use of valproate in women of childbearing potential who cannot be treated with other medicines is in accordance with the Pregnancy Prevention Programme (PPP). Given these and other risks of valproate, these measures also aim to reduce initiation of valproate to only in patients for whom no other therapeutic options are suitable.

The regulatory change in January 2024, for oral valproate medicines, means that:

A. Valproate must not be started in new patients (male or female) younger than 55 years, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.

B. At their next annual specialist review, women of childbearing potential and girls should be reviewed using a revised valproate Risk Acknowledgement Form, which will include the need for a second specialist signature if the patient is to continue with valproate and subsequent annual reviews with one specialist unless the patient's situation changes

Advise leaders that current safety measures for valproate continue to apply, including the valproate PPP for any girls and women of childbearing potential. See December 2022 Drug Safety Update for further information, including advice for clinicians to consider all other suitable therapeutic options before newly prescribing valproate in patients younger than 55.

Advise leaders in general practice and pharmacy that teams should continue to prescribe and dispense valproate but also discuss the current warnings and upcoming measures relating to valproate with their patients and consider together how it affects the patient's individual circumstances. New educational materials should be integrated into local guidance to ensure patients are able to make an informed choice.

Actions required

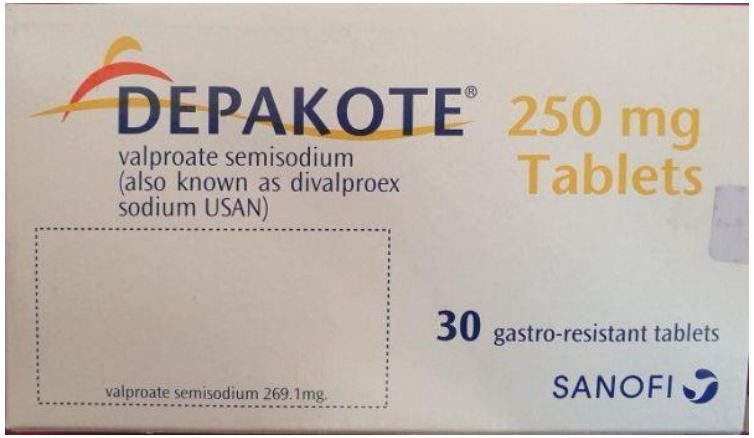
When: To begin as soon as possible and be completed by **31 January 2024**

1. Designate a new or existing group to co-ordinate the implementation of the new regulatory measures in providers, with oversight from a senior quality group. This group should include (but is not restricted to):
   a. An appointed chair with delegated responsibility for the actions in this alert.
   b. Representation from clinical leads in all the specialities named above and any other relevant departments.
   c. A mechanism by which the group can involve and be informed by patients with lived experience.
2. The group should be tasked with, and document, progress towards:
   a. Updating all local guidance and protocols relating to prescribing of valproate to reflect the new regulatory position, including definitions of the roles and responsibilities of clinicians and provider organisations, and the recording of compliance with the risk forms
   b. Commissioning work if necessary to understand the needs of the affected population, including those people most at risk of health inequalities.
   c. Reviewing the results of local audit(s) of compliance with the existing PPP measures for girls and women of childbearing potential prescribed valproate.
   d. Commissioning/determining the local pathways of care for women of childbearing potential and girls in relation to the prescribing and review of valproate.
   e. Planning for and identification of clinical resource to meet the identified needs of the population and implement the new regulatory measures.
3. Based upon the findings of the above, the group should produce an Action and Improvement Plan by the alert deadline that is communicated with all relevant staff to ensure smooth implementation of the new regulatory measures and to allow for continuous improvement in care of patients who are considering or being prescribed valproate, including ongoing improvement, monitoring and audit.

For any enquiries about this alert contact: info@mhra.gov.uk 1/2

To learn more on how alert issuing bodies are working together to issue alerts please go to https://www.england.nhs.uk/patient-safety/national-patient-safety-alerting-committee/

Valproate safety measures

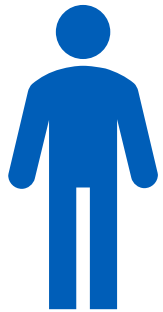


Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell▼) regulatory changes are further supported by:

- smaller pack sizes to encourage monthly prescribing
- a pictogram/warning image on valproate labelling
- rules introduced in 2023 to ensure all patients receive the whole pack of valproate with the warnings on the box

Valproate risks to babies and children

Valproate is associated with a significant risk of birth defects and developmental disorders



≈ 1 in 9 babies are at risk of a physical birth abnormality

General population	2 to 3 out of 100 babies
Valproate	**About 10 out of 100 babies**
Phenobarbital	6 to 7 out 100 babies
Phenytoin	About 6 out of 100 babies
Topiramate	4 to 5 out of 100 babies
Carbamazepine	4 to 5 out of 100 babies

MHRA (2024) Valproate use by women and girls
MHRA (2021) Antiepileptic drug: review of safety of use during pregnancy

≅ 4 in 10 children are at risk of developmental disorders

General population	About 3 to 4 out of 100
Valproate	**About 3 to 4 out of 10 children**

The effects on development can include:
- being late in learning to walk and talk
- lower intelligence than other children of the same age
- poor speech and language skills
- memory problems.

MHRA (2024) Valproate use by women and girls
Annual Report of the Chief Medical Officer (2012) Our Children Deserve Better: Prevention Pays

1 in 20 children are at are at risk of developmental disorders

General population	About 3 to 4 out of 100
Valproate	**5 out of 100 children**

The types of neurodevelopmental disorders observed include:
- autism spectrum disorder
- intellectual disability
- communication disorder
- attention deficit hyperactivity disorder, movement disorders

MHRA (2024) Visual risk communication diagram to be used by a healthcare professional when counselling on the risks
Annual Report of the Chief Medical Officer (2012) Our Children Deserve Better: Prevention Pays

Valproate safety update

Safety requirement	Men and boys of reproductive potential	Women and girls of childbearing potential
Valproate use	Should not be started in patients aged under 55 years unless two specialists consider and document that there is no other effective or tolerated treatment or the risk of infertility or potential risk of testicular toxicity do not apply	Must not be started in new patients younger than 55 years, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply
Contraindications (excluding clinical contraindications detailed in the BNF)	***Precautionary advice*** to not donate sperm during treatment with valproate and for three months after stopping valproate	Must not be used unless the conditions of the Pregnancy Prevention Programme are met Must not be used in pregnancy for migraine prophylaxis [unlicensed] and bipolar disorder; BUT it must only be considered for epilepsy if there is no suitable alternative treatment

Valproate safety update

Safety requirement	Men and boys of reproductive potential	Women and girls of childbearing potential
Treatment risks	Risk of infertility and neurodevelopmental disorders in children	Risk of physical birth abnormality and neurodevelopmental disorders in children
Risk minimisation tool	Risk acknowledgment Form (RAF) – New initiations only	Annual risk acknowledgement form (ARAF) – New initiations and existing patients
Specialist counter signatories	Two specialists must sign the form for new patients initiating valproate under 55 years of age, but it is not be required for men (or males) currently taking valproate.	Two specialists must sign the form for new patients initiating valproate under 55 years of age and thereafter annual review and ARAF completion with a single signature is required
Annual treatment review	No mandatory annual specialist review but may require specialist review where applicable as part of usual care	Annual **specialist** review required for all female patients on valproate to reassess treatment need and risks

Valproate safety update

Safety requirement	Men and boys of reproductive potential	Women and girls of childbearing potential
Contraception	Patient and sexual partner of childbearing potential should both use effective birth control (condoms and another form of female contraception) as a precaution and for at least 3 months after stopping valproate	Highly effective methods (typical-use failure rates of less than 1%) female sterilisation and long-acting reversible contraceptive (LARC) methods (intrauterine devices and implants)
Patient information	Patient guide Advice for male patients on valproate to use contraception	Patient guide Patient card Decision tool: to guide decisions about taking valproate for epilepsy Decision tool: to guide decisions about taking valproate for bipolar disorder

Pregnancy Prevention Programme (PPP)

prevent valproate pregnancy prevention programme **essentially comprises:**

- Discussing the risks of pregnancy with patients / responsible person
- Serum pregnancy test before first prescription
- Arrange use of effective contraception (most likely IUD or implant) before first prescription and then on an ongoing basis
- Completion of an Annual Risk Acknowledgement Form by the patient or their responsible person / parent
- A minimum of annual specialist review
- Providing a copy of the Patient Guide to the patient (or parent/caregiver/responsible person)

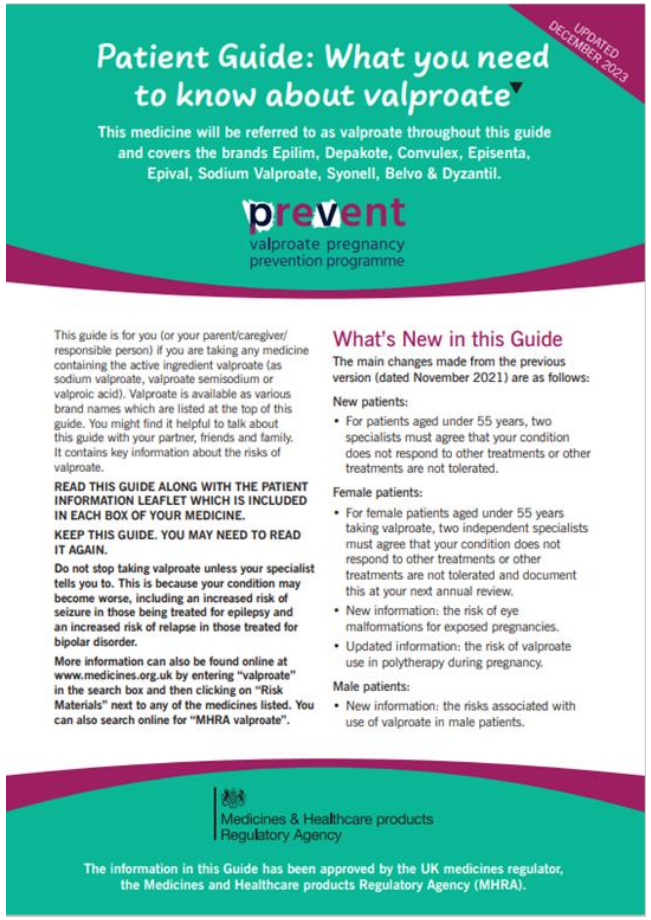
Pregnancy Prevention Programme (PPP)

Role of general practitioners

Refer new patients to a specialist for diagnosis and treatment initiation.

Follow up with each female patient after their specialist review, especially if they are on valproate, to ensure:

- They have the **Patient Guide** and a signed Annual Risk Acknowledgment Form in their medical records.
- They are using **effective contraception** and understand its importance throughout valproate treatment, including pregnancy testing if needed.
- Remind them to **contact you immediately if there's any issue with contraception or a possible pregnancy**.
- For children on valproate, **ensure the responsible person contacts the GP once the patient has their first period, so the GP can refer the patient back to the specialist**.



UPDATED DECEMBER 2023

Patient Guide: What you need to know about valproate

This medicine will be referred to as valproate throughout this guide and covers the brands Epilim, Depakote, Convulex, Episenta, Epival, Sodium Valproate, Syonell, Belvo & Dyzantil.

prevent
valproate pregnancy prevention programme

This guide is for you (or your parent/caregiver/ responsible person) if you are taking any medicine containing the active ingredient valproate (as sodium valproate, valproate semisodium or valproic acid). Valproate is available as various brand names which are listed at the top of this guide. You might find it helpful to talk about this guide with your partner, friends and family. It contains key information about the risks of valproate.

READ THIS GUIDE ALONG WITH THE PATIENT INFORMATION LEAFLET WHICH IS INCLUDED IN EACH BOX OF YOUR MEDICINE.

KEEP THIS GUIDE. YOU MAY NEED TO READ IT AGAIN.

Do not stop taking valproate unless your specialist tells you to. This is because your condition may become worse, including an increased risk of seizure in those being treated for epilepsy and an increased risk of relapse in those treated for bipolar disorder.

More information can also be found online at www.medicines.org.uk by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines listed. You can also search online for "MHRA valproate".

What's New in this Guide

The main changes made from the previous version (dated November 2021) are as follows:

New patients:

- For patients aged under 55 years, two specialists must agree that your condition does not respond to other treatments or other treatments are not tolerated.

Female patients:

- For female patients aged under 55 years taking valproate, two independent specialists must agree that your condition does not respond to other treatments or other treatments are not tolerated and document this at your next annual review.
- New information: the risk of eye malformations for exposed pregnancies.
- Updated information: the risk of valproate use in polytherapy during pregnancy.

Male patients:

- New information: the risks associated with use of valproate in male patients.

Medicines & Healthcare products Regulatory Agency

The information in this Guide has been approved by the UK medicines regulator, the Medicines and Healthcare products Regulatory Agency (MHRA).

Contraception

Women and girls of childbearing potential

- Optimal choice is highly effective method (user independent) that have typical-use failure rates of less than 1% and include the long-acting reversible contraceptives (LARC):
    - copper intrauterine device (Cu-IUD),
    - levonorgestrel intrauterine system (LNG-IUS),
    - progestogen-only implant (IMP), and
    - Sterilisation,

If a user-independent form is not used, **two complementary forms of contraception including a barrier method** should be used and regular pregnancy testing considered.

Men and boys of reproductive potential

- It is recommended that patients and sexual partners of childbearing potential should both use effective birth control (condoms and another form of contraception) **as a precaution** while taking valproate and for at least 3 months after stopping valproate.

Ways to access contraception vary

- Specialist referral to community or hospital sexual health services.
- Specialist referrals to gynaecology when assessing the appropriateness of valproate.
- Recommendation to the patient to use two complementary methods of contraception and to discuss with the GP.

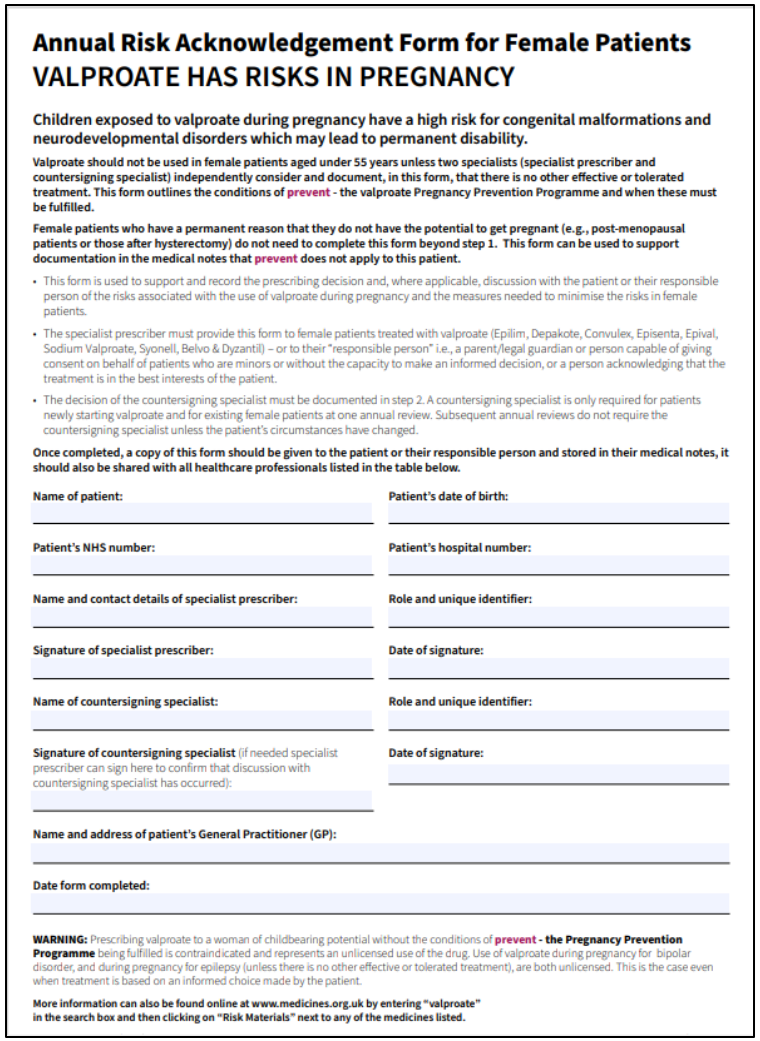
Annual Risk Acknowledgement Form (ARAF)

Document completed by the specialist overseeing the Pregnancy Prevention Programme for new and existing women and girls of reproductive potential

The ARAF has four steps to the form:

- Step 1: specialist to determine if the patient is at risk of reproductive harms of valproate
- Step 2: specialist and countersigning specialist to state their prescribing decision.
- Step 3: specialist prescriber to explain the risks to patient
- Step 4: needs to be completed by the patient before enrolment onto 'PREVENT'

ARAF is completed at each annual specialist review.



Annual Risk Acknowledgement Form for Female Patients
VALPROATE HAS RISKS IN PREGNANCY

Children exposed to valproate during pregnancy have a high risk for congenital malformations and neurodevelopmental disorders which may lead to permanent disability.

Valproate should not be used in female patients aged under 55 years unless two specialists (specialist prescriber and countersigning specialist) independently consider and document, in this form, that there is no other effective or tolerated treatment. This form outlines the conditions of prevent - the valproate Pregnancy Prevention Programme and when these must be fulfilled.

Female patients who have a permanent reason that they do not have the potential to get pregnant (e.g., post-menopausal patients or those after hysterectomy) do not need to complete this form beyond step 1. This form can be used to support documentation in the medical notes that prevent does not apply to this patient.

- This form is used to support and record the prescribing decision and, where applicable, discussion with the patient or their responsible person of the risks associated with the use of valproate during pregnancy and the measures needed to minimise the risks in female patients.
- The specialist prescriber must provide this form to female patients treated with valproate (Epilim, Depakote, Convulex, Episenta, Epival, Sodium Valproate, Syonell, Belvo & Dyzantil) – or to their "responsible person" i.e., a parent/legal guardian or person capable of giving consent on behalf of patients who are minors or without the capacity to make an informed decision, or a person acknowledging that the treatment is in the best interests of the patient.
- The decision of the countersigning specialist must be documented in step 2. A countersigning specialist is only required for patients newly starting valproate and for existing female patients at one annual review. Subsequent annual reviews do not require the countersigning specialist unless the patient's circumstances have changed.

Once completed, a copy of this form should be given to the patient or their responsible person and stored in their medical notes, it should also be shared with all healthcare professionals listed in the table below.

Name of patient: | **Patient's date of birth:**

Patient's NHS number: | **Patient's hospital number:**

Name and contact details of specialist prescriber: | **Role and unique identifier:**

Signature of specialist prescriber: | **Date of signature:**

Name of countersigning specialist: | **Role and unique identifier:**

Signature of countersigning specialist (if needed specialist prescriber can sign here to confirm that discussion with countersigning specialist has occurred): | **Date of signature:**

Name and address of patient's General Practitioner (GP):

Date form completed:

WARNING: Prescribing valproate to a woman of childbearing potential without the conditions of **prevent - the Pregnancy Prevention Programme** being fulfilled is contraindicated and represents an unlicensed use of the drug. Use of valproate during pregnancy for bipolar disorder, and during pregnancy for epilepsy (unless there is no other effective or tolerated treatment), are both unlicensed. This is the case even when treatment is based on an informed choice made by the patient.

More information can also be found online at www.medicines.org.uk by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines listed.

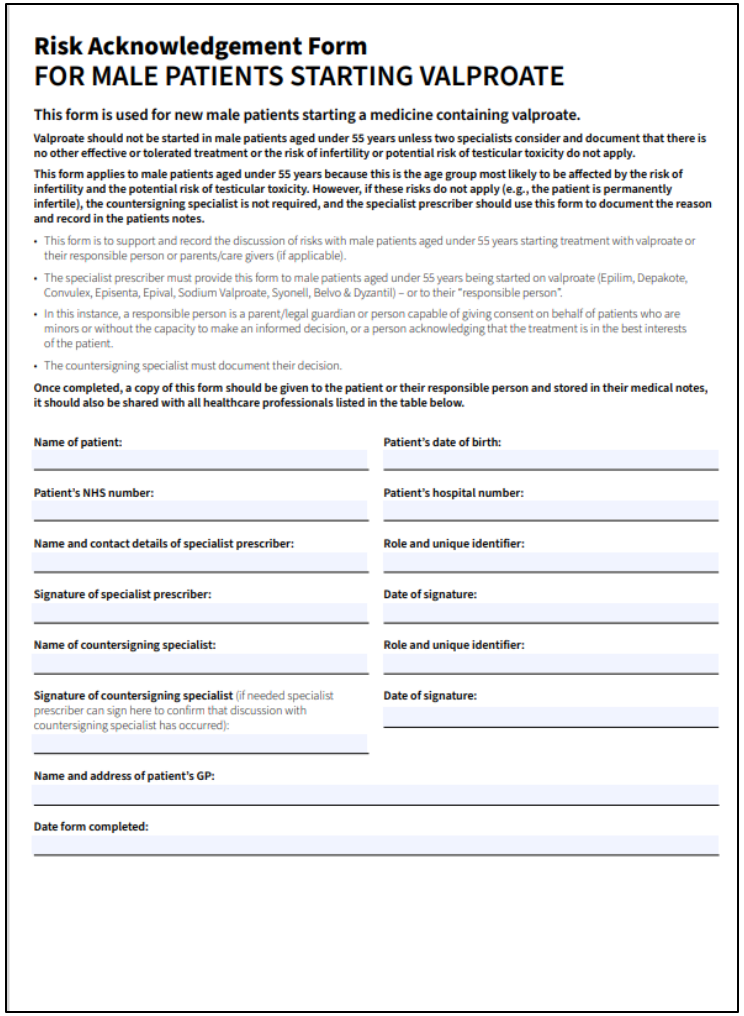
Risk Acknowledgement Form (RAF)

Newly started men and boys of reproductive potential

- Specialist initiating will complete Risk Acknowledgement Form for male patients starting valproate:
  - Used to support and record the discussion between the patient and specialist prescriber of the risks associated with valproate in when starting treatment with valproate and to record the decision of the countersigning specialist.
  - **This currently only needs to be completed by a specialist at initiation of valproate in new patients.**

Existing men and boys of reproductive potential

- MHRA issued a reminder in February 2025 that two signatories (e.g. RAF) are not required.
- At the next face to face (in person) scheduled/routine medication review, clinicians can use the updated MHRA patient guide to facilitate a discussion about potential reproductive risks.
- Further information available in the NEL guidance note GP-actions-for-Valproate-in-male-patients-Sept-2024.pdf.



Risk Acknowledgement Form
FOR MALE PATIENTS STARTING VALPROATE

This form is used for new male patients starting a medicine containing valproate.

Valproate should not be started in male patients aged under 55 years unless two specialists consider and document that there is no other effective or tolerated treatment or the risk of infertility or potential risk of testicular toxicity do not apply.

This form applies to male patients aged under 55 years because this is the age group most likely to be affected by the risk of infertility and the potential risk of testicular toxicity. However, if these risks do not apply (e.g., the patient is permanently infertile), the countersigning specialist is not required, and the specialist prescriber should use this form to document the reason and record in the patients notes.

- This form is to support and record the discussion of risks with male patients aged under 55 years starting treatment with valproate or their responsible person or parents/care givers (if applicable).
- The specialist prescriber must provide this form to male patients aged under 55 years being started on valproate (Epilim, Depakote, Convulex, Episenta, Epival, Sodium Valproate, Syonell, Belvo & Dyzantil) – or to their "responsible person".
- In this instance, a responsible person is a parent/legal guardian or person capable of giving consent on behalf of patients who are minors or without the capacity to make an informed decision, or a person acknowledging that the treatment is in the best interests of the patient.
- The countersigning specialist must document their decision.

Once completed, a copy of this form should be given to the patient or their responsible person and stored in their medical notes, it should also be shared with all healthcare professionals listed in the table below.

Name of patient: | **Patient's date of birth:**

Patient's NHS number: | **Patient's hospital number:**

Name and contact details of specialist prescriber: | **Role and unique identifier:**

Signature of specialist prescriber: | **Date of signature:**

Name of countersigning specialist: | **Role and unique identifier:**

Signature of countersigning specialist (if needed specialist prescriber can sign here to confirm that discussion with countersigning specialist has occurred): | **Date of signature:**

Name and address of patient's GP:

Date form completed:

NHS
North East London

NEL valproate safety dashboard

DEMO

Welcome

NHS North East London

Valproate, also known as sodium valproate, valproic acid and valproate semi-sodium, is used as a treatment for epilepsy, bipolar disorders, and other indications. It is an active ingredient licensed under several brand names and generic sodium valproate. A National Patient Safety Alert (NatPSA) was introduced in January 2024 to ask clinicians to implement new measures to reduce the harms of valproate. In September 2024, due to new evidence of possible harms of valproate in men, the MHRA has issued new safety measures to further support prescribers around the safe use of valproate in all men and their partners

Risk in girls and women of childbearing potential

The Medicines & Healthcare products Regulatory Agency (MHRA) now states in valproate safety measures that in women and girls of childbearing potential, if valproate is taken during pregnancy, up to 4 in 10 babies are at risk of developmental disorders and approximately 1 in 10 are at risk of birth defects.

Responding to concerns that some women were not aware if the risks when used in pregnancy, the MHRA now advise that valproate must not be used in any women or girl able to have children unless there is a pregnancy prevention programme (PPP) in place, also known as 'PREVENT'

There are specific conditions that patients of 'childbearing potential' should meet if participating in the programme. The patient 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.

DEMO

Potential risk in boys and men of reproductive potential

The MHRA advices, in men and boys of reproductive potential valproate taken around the time of conception was associated with 5 out of 100 children being diagnosed with a neurodevelopmental disorder.
As a precaution, men prescribed valproate and their partners should use effective contraception and those planning a family within the next year should speak to a healthcare professional about their treatment options.
Please note any specialist initiating valproate in males must complete a Risk Acknowledge Form (RAF) at initiation and a second independent specialist must confirm that there is no other effective or tolerated treatment.

Purpose of the dashboard

The dashboard aims to support and assure the safe use of valproate and minimise the teratogenic risk of valproate to patients of childbearing and reproductive potential, by showing the

- Number of girls and women of child bearing potential with valid annual Risk Acknowledgement Form (ARAF) completed.
- Number of boys and men of reproductive potential with a completed risk acknowledgment form (RAF).
- Prevention Prevention Programme (PPP) status for girls and women of childbearing potential.
- Up to date on a Pregnancy Prevention Programme (PPP).

The dashboard will identify and stratify patients of childbearing potential prescribed valproates by their NEL GPs based on adherence to MHRA safety guidelines and the patient's risk of becoming pregnant. It should incorporate the identity of the specialist secondary or mental health Trusts managing the care of the patient for specific indications and specialists related to valproate use or taking valproate containing medicines, to enable clinicians and pharmacists to monitor, review and manage our patients, within NEL.
The dashboard has been developed in compliance with the NatPSA Safety Alert, to establish a NEL-wide dashboard / registry, to identify, review, manage and monitor all women and girls of childbearing potential and boys and men of reproductive potential under the age of 55 years of age prescribed valproate.

Overview of the proposed process

All the indicators are based on SNOMED coded data which is collected at Practice level and aggregated at NEL level. To support data quality assurance, it is important for practices to keep the patient's electronic health record up to date.

Valproate Annual Risk Acknowledgment - ARAF

2,236,625
List Size

Please note Valproate Medication looks for data points at given time, 2015 onwards unlike Annual Risk Acknowledge (ARAF) and Pregnancy Prevention Program (PPP) which is limited to last 12 months

NHS North East London

TESTING

Summary : Data is limited to the last 12 months Monday, 1 April 2024 **to** Monday, 31 March 2025 **except for Valproate Medications, where medications are picked at any point of time starting from 2015 onwards**

Borough DEMO

All

PCN

All

GP Practice

All

Age Band

All

Ethnicity

All

Gender

All

EMIS / System One

All

Monday, 31 March 2025
Last Updated

Valproate Annual Risk Acknowledge / Pregnancy Prevention Program measures

Valproate Annual Risk Acknowledge - ARAF	315
Patients with Pregnancy Prevention Program	263
Patients with ARAF and having Learning Disability	113
Patients with ARAF Form and having A&E Attendance	99
Patients with ARAF and having an admission	72
Patients with ARAF and having an Outpatient appointment	196

Valproate Medication measures

Patients with Valproate Medication	11,794
Patients on Valproate Medication and ARAF	279
Patients on Valproate Medication and PPP	117

DEMO

Snomed Codes and Activity Counts

Snomed Code	Snomed Description	Patients with ARAF
^ESCT1433401	Valproate ARAF (Annual Risk Acknowledgement Form) completed	0
Y362e	Valproate Annual Risk Acknowledgement Form completed	0
1366401000000107	Valproate Annual Risk Acknowledgement Form completed (situation)	136
^ESCT1433400	Valproate Annual Risk Acknowledgement Form completed	142

DEMO

NHS
North East London

Resources for healthcare professionals and patients

Local resources

Guidance notes outlining actions for clinicians in primary and secondary care in response to medicines safety related national patient safety alerts and drug safety updates.

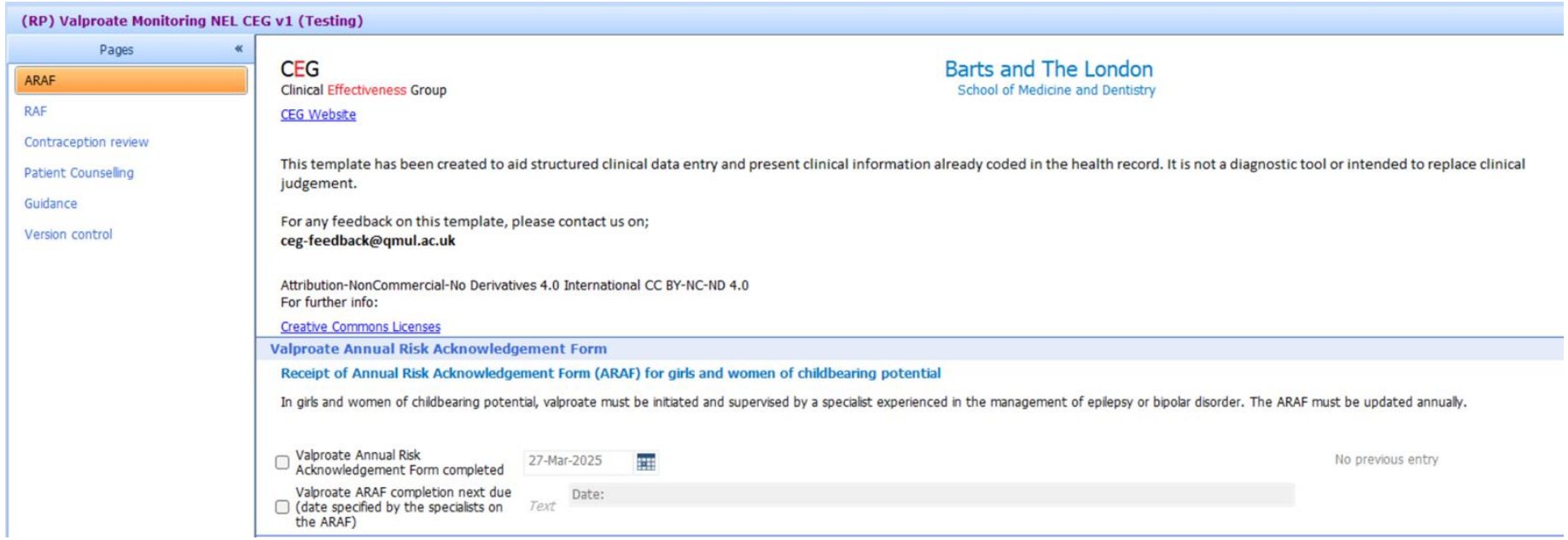
Valproate safety dashboard and templates (EMIS and SystmOne) to support patient identification and implementation measures to mitigate risk of harm to girls and women of childbearing potential and boys and men of reproductive potential.

OptimiseRx valproate safety messages that warn clinicians about teratogenic risks and support adherence to regulatory measures (e.g. PPP, ARAF, RAF)

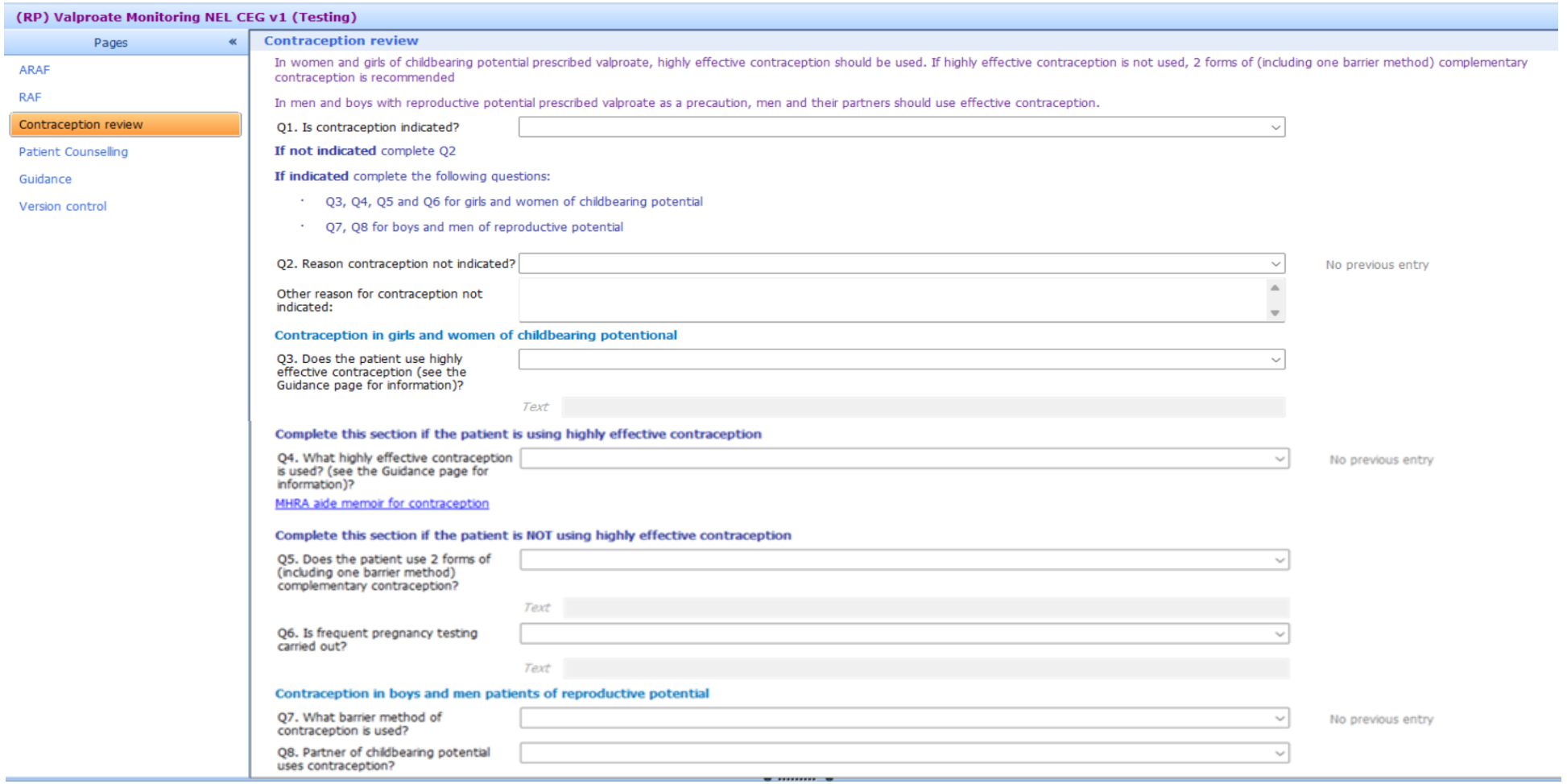
TMSIG will identify deliverables and initiatives that would benefit from a whole system ‘do once approach’ and facilitate co-delivery e.g. FAQs/factsheet on contraception for patients prescribed valproate (coming soon).

TMSIG aims to co-ordinate a standardised approach to medicines safety related national patient safety alerts or local incidents involving medicines with teratogenic potential.

NEL Valproate monitoring template

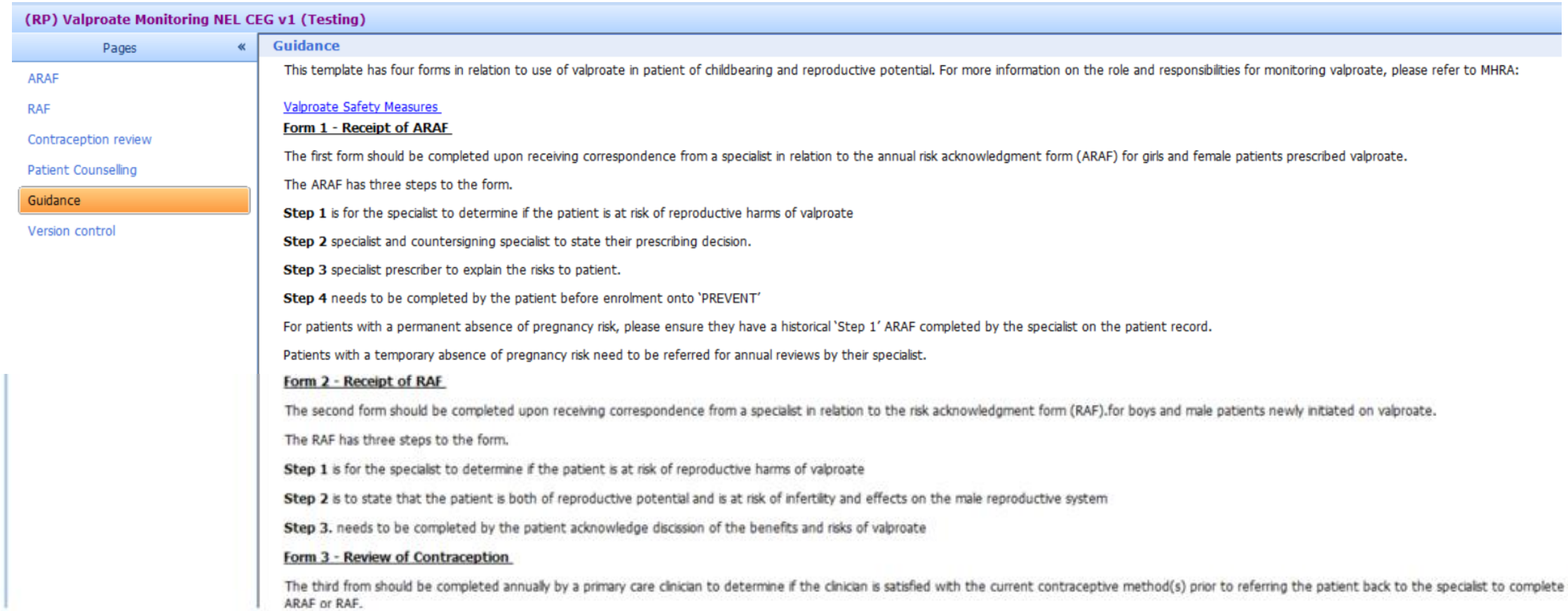


NEL Valproate monitoring template



NEL Valproate monitoring template

NEL Valproate monitoring template



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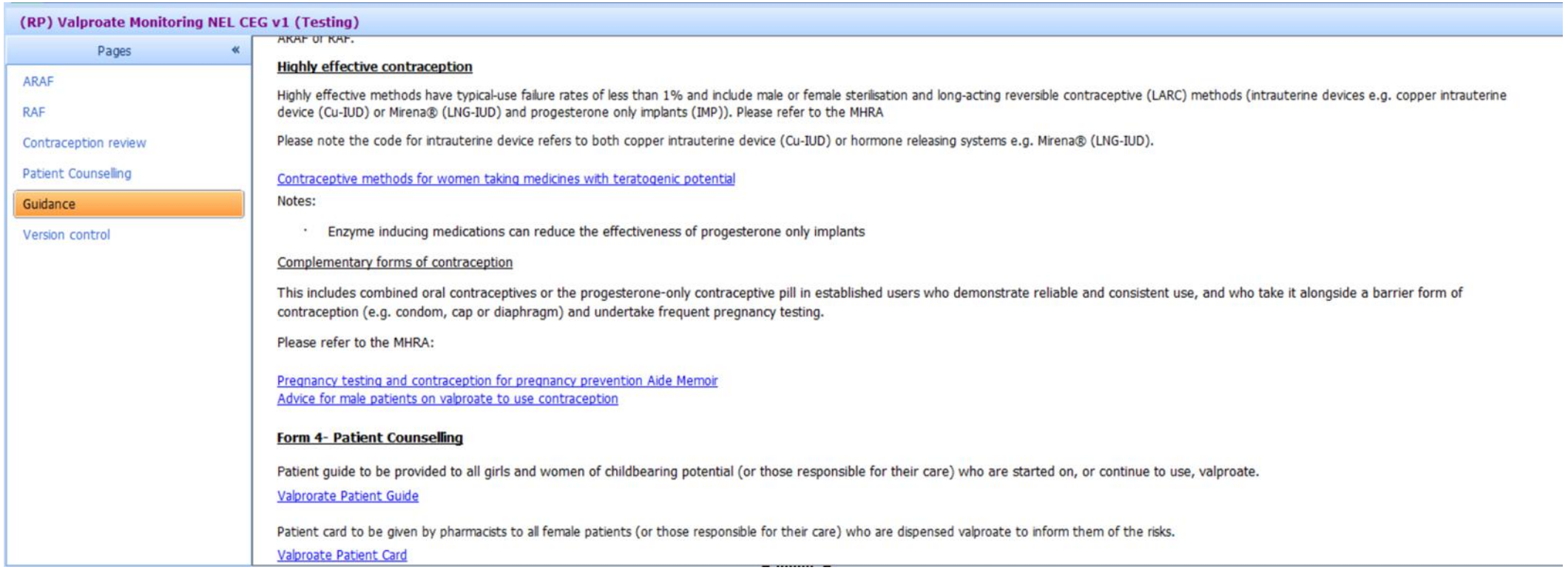
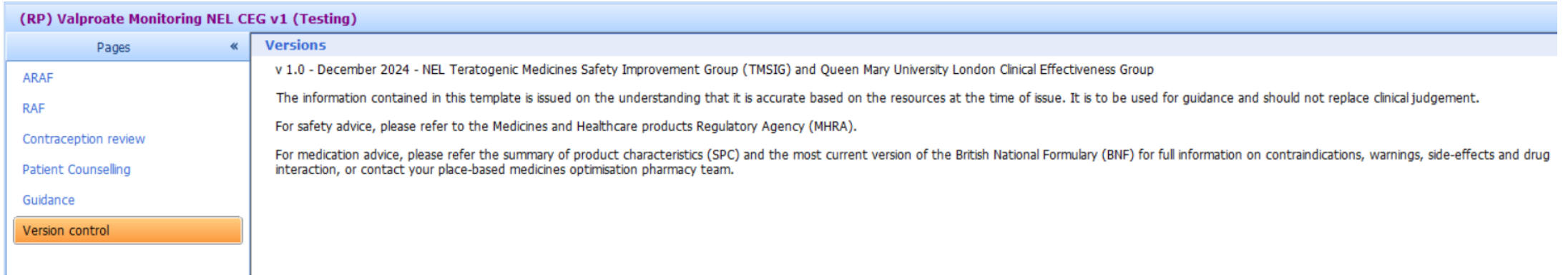
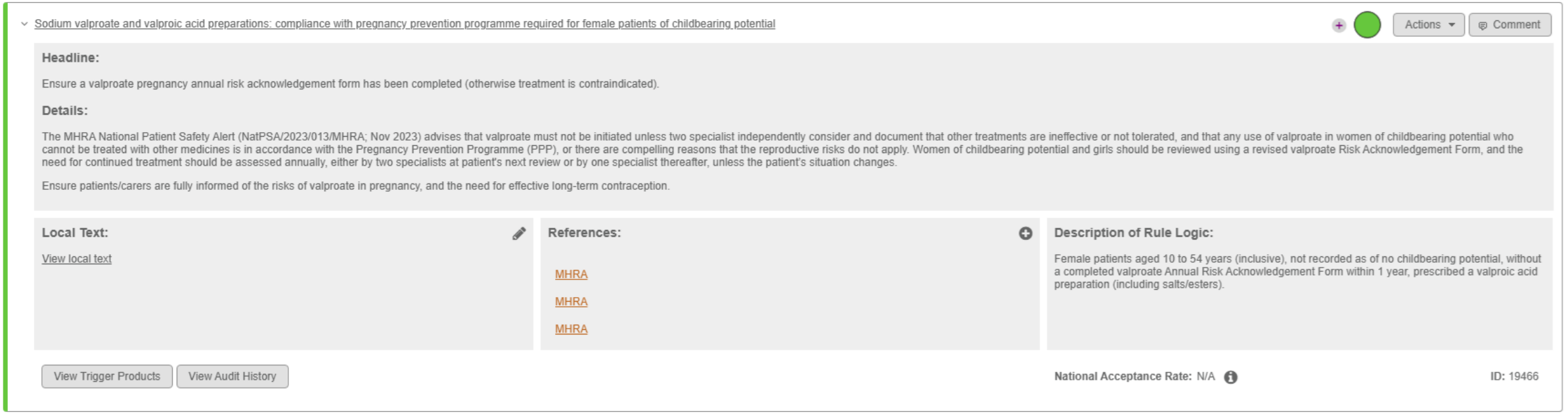


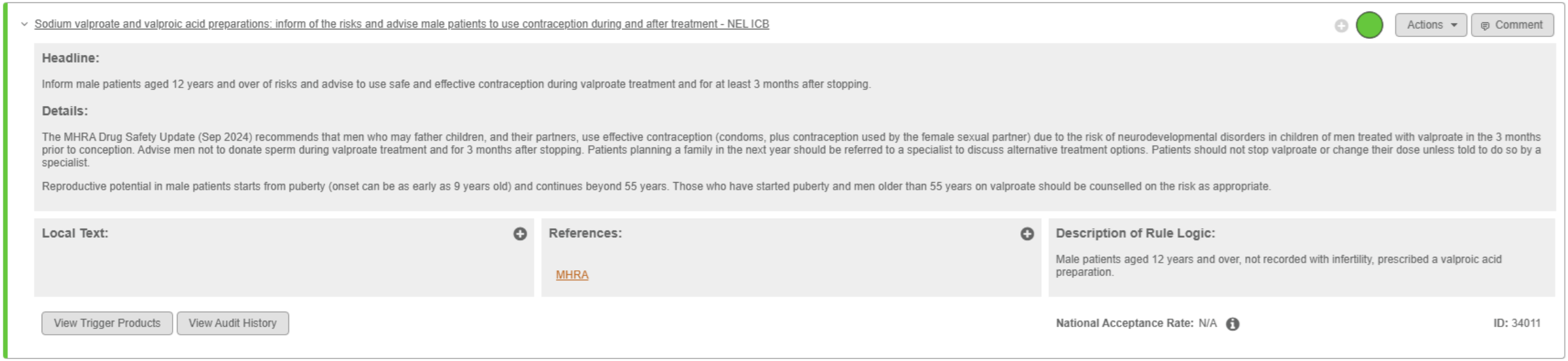
NEL Valproate monitoring template



OptimiseRx


Sodium valproate and valproic acid preparations: compliance with pregnancy prevention programme required for female patients of childbearing potential
Actions
Comment
Headline:
Ensure a valproate pregnancy annual risk acknowledgement form has been completed (otherwise treatment is contraindicated).
Details:
The MHRA National Patient Safety Alert (NatPSA/2023/013/MHRA; Nov 2023) advises that valproate must not be initiated unless two specialist independently consider and document that other treatments are ineffective or not tolerated, and that any use of valproate in women of childbearing potential who cannot be treated with other medicines is in accordance with the Pregnancy Prevention Programme (PPP), or there are compelling reasons that the reproductive risks do not apply. Women of childbearing potential and girls should be reviewed using a revised valproate Risk Acknowledgement Form, and the need for continued treatment should be assessed annually, either by two specialists at patient's next review or by one specialist thereafter, unless the patient's situation changes.
Ensure patients/carers are fully informed of the risks of valproate in pregnancy, and the need for effective long-term contraception.
Local Text:
View local text
References:
MHRA
MHRA
MHRA
Description of Rule Logic:
Female patients aged 10 to 54 years (inclusive), not recorded as of no childbearing potential, without a completed valproate Annual Risk Acknowledgement Form within 1 year, prescribed a valproic acid preparation (including salts/esters).
View Trigger Products
View Audit History
National Acceptance Rate: N/A
ID: 19466

OptimiseRx


Sodium valproate and valproic acid preparations: inform of the risks and advise male patients to use contraception during and after treatment - NEL ICB
Actions
Comment
Headline:
Inform male patients aged 12 years and over of risks and advise to use safe and effective contraception during valproate treatment and for at least 3 months after stopping.
Details:
The MHRA Drug Safety Update (Sep 2024) recommends that men who may father children, and their partners, use effective contraception (condoms, plus contraception used by the female sexual partner) due to the risk of neurodevelopmental disorders in children of men treated with valproate in the 3 months prior to conception. Advise men not to donate sperm during valproate treatment and for 3 months after stopping. Patients planning a family in the next year should be referred to a specialist to discuss alternative treatment options. Patients should not stop valproate or change their dose unless told to do so by a specialist.
Reproductive potential in male patients starts from puberty (onset can be as early as 9 years old) and continues beyond 55 years. Those who have started puberty and men older than 55 years on valproate should be counselled on the risk as appropriate.
Local Text:
References:
MHRA
Description of Rule Logic:
Male patients aged 12 years and over, not recorded with infertility, prescribed a valproic acid preparation.
View Trigger Products
View Audit History
National Acceptance Rate: N/A
ID: 34011

National resources

Healthcare professionals

- Healthcare Professional Guide: Provides updated information for healthcare professionals on the risks of valproate in pregnancy and the risks for male patients, the new conditions for valproate prescribing and key discussions points
- MHRA Pregnancy testing and contraception for pregnancy prevention during treatment with medicines of teratogenic potential (2024)
- FSRH statement: Contraception for women using known teratogenic drugs (Feb 2018)
- Full pack dispensing of valproate-containing medicines: Provides guidance for dispensing of valproate-containing medicines in the manufacturer's original full pack, following amendments to the Human Medicines Regulations (HMRs)
- Pharmacy poster: Provides important actions for pharmacists dispensing valproate to female patients.
- Valproate 'White Box' warning labels Templates for warning Labels with Valproate Pregnancy Pictogram for Pharmacy to use with white box dispensing in exceptional circumstances for dispensary use only.

National resources

Healthcare professionals

- Risk minimisation measures required for valproate prescribing in girls and women aged under 55 years
- Risk minimisation measures required for valproate prescribing in boys and men aged under 55 years
- Risk minimisation measures required for valproate prescribing in women and men aged over 55 years
- Visual risk communication diagram to be used by a healthcare professional when counselling on the risks to male patients
- Discussing the risks of sodium valproate - ethical learning material - GMC
- Sodium Valproate resources and information | General Pharmaceutical Council
- High risk medicines: valproate - Care Quality Commission

National resources

Patients and carers

- Patient guide: with information on the risks of valproate in pregnancy and the risks to male patients and what they need to do.
- Patient card: Provides key information for female patients receiving valproate on contraception and pregnancy prevention.
- Decision tool: Tool for women and girls of childbearing potential with epilepsy a support tool to guide decisions about taking valproate.
- Decision tool: Tool for women and girls of childbearing potential with bipolar a support tool to guide decisions about taking valproate.
- Advice for male patients on valproate to use contraception
- Sodium Valproate - Epilepsy Society
- Valproate Mood Stabiliser - Mind

NHS
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Patient case

What would you do?

GP/practice pharmacist receives a repeat prescription request for sodium valproate from Millie, who is new to the practice. She sees that a valproate Annual Risk Acknowledgement Form (ARAF) has not been completed.

After reviewing Millie's medical record, GP/practice pharmacist becomes concerned because it appears that:

- Millie has been prescribed valproate continuously since 2010
- she hasn't seen a neurologist since 2012
- she doesn't appear to be on the pregnancy prevention programme (PPP).
- In Millie's medical record GP/practice pharmacist reads that Millie has given birth to two children. She wonders whether Millie has ever been advised about the risks of taking valproate during pregnancy. She notes that Millie's two children were both born before 2018 when the MHRA's strengthened regulatory position came into force, and before the MHRA issued additional regulatory measures in 2023

Case reflections

Under the current MHRA regulatory measures it is the responsibility of GPs/prescribing primary care clinicians to make sure, each time a repeat prescription is issued, that people of childbearing potential on valproate:

- Are fulfilling the requirements of a PPP
- Are having an annual review with a specialist.
- Have an up to date, signed, Annual Risk Acknowledgement Form (ARAF)
- Are aware of the risks of valproate, if taken during pregnancy
- Are using effective contraception
- Have been given the valproate patient guide, or know how to access it online
- Know they must contact their GP urgently for a referral to a specialist if pregnant

Further details can be found at Discussing the risks of sodium valproate - ethical learning material - GMC

NHS
North East London

Actions for primary care

Actions for contraception

Specialists

•Ensure the patient understands the need to comply with effective contraception throughout treatment and undergo pregnancy testing when required
•Refer for contraception advice as needed

Primary care prescribing clinicians

•Ensure the patient is using effective contraception and understands the need to comply with effective contraception throughout treatment with valproate and undergo pregnancy testing when required
- Remind the patient to contact you immediately if they suspect there has been a problem with their contraception or if they may be pregnant
- Inform patients who are planning to get pregnant to not stop contraception or valproate until told to by their specialist prescriber.

Community pharmacists

•Confirm with the patient they have been made aware to always use effective contraception and to see their GP to be urgently referred to their specialist, should they be planning a pregnancy.

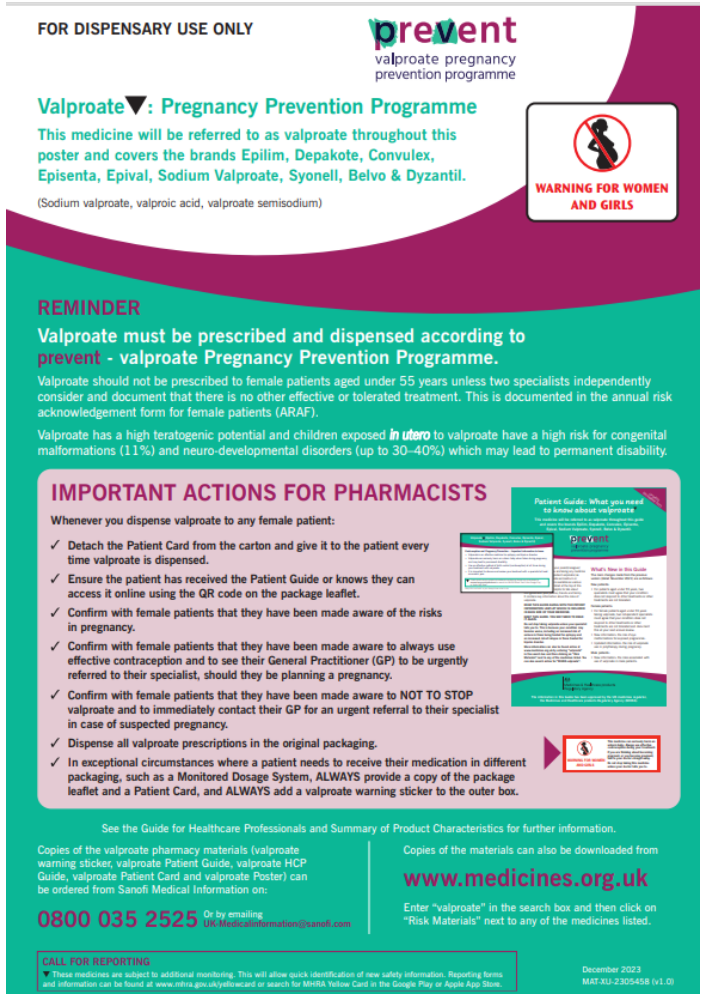
Actions for the primary care prescribing clinician

- Ensure the EMIS or SystmOne template "**Valproate Monitoring NEL CEG**" has been completed to ensure the appropriate SNOMED codes have been applied; also ensure that a code associated with the diagnosis has been applied.
- Check if the patient has been given the valproate patient guide, or know how to access it online
- For women and girls of childbearing potential prescribe within the remit of the pregnancy prevention programme (PREVENT), ensuring that:
    - The practice has received a valid ARAF (i.e., completed within the previous year).
    - The patient is aware of the risks of valproate, if taken during pregnancy
    - 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)
    - The patient is using highly effective contraception (or complementary methods), if indicated.
    - Continue prescriptions throughout the valid ARAF period

Actions for the primary care prescribing clinician

- Refer women and girls of childbearing potential who have an expired, expiring, or absent ARAF as soon as practicable back to the specialist (if a referral is not already completed or specialist review is not already arranged) for a review and completion of a new ARAF.
- If a women and girls of childbearing potential have 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 the patient
  - 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
- For men and boys of reproductive potential newly initiated on valproate ensure they have a valid RAF

Actions for community pharmacists



FOR DISPENSARY USE ONLY

prevent
valproate pregnancy prevention programme

Valproate▼: Pregnancy Prevention Programme

This medicine will be referred to as valproate throughout this poster and covers the brands Epilim, Depakote, Convulex, Episenta, Epival, Sodium Valproate, Syonell, Belvo & Dyzantil.

(Sodium valproate, valproic acid, valproate semisodium)

WARNING FOR WOMEN AND GIRLS

REMINDER

Valproate must be prescribed and dispensed according to prevent - valproate Pregnancy Prevention Programme.

Valproate should not be prescribed to female patients aged under 55 years unless two specialists independently consider and document that there is no other effective or tolerated treatment. This is documented in the annual risk acknowledgement form for female patients (ARAF).

Valproate has a high teratogenic potential and children exposed *in utero* to valproate have a high risk for congenital malformations (11%) and neuro-developmental disorders (up to 30–40%) which may lead to permanent disability.

IMPORTANT ACTIONS FOR PHARMACISTS

Whenever you dispense valproate to any female patient:

- ✓ Detach the Patient Card from the carton and give it to the patient 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 female patients that they have been made aware of the risks in pregnancy.
- ✓ Confirm with female patients 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 female patients that they have been made aware to NOT TO STOP valproate and to immediately contact their GP for an urgent referral to their specialist in case of suspected pregnancy.
- ✓ Dispense all valproate prescriptions in the original packaging.
- ✓ In exceptional circumstances where a patient needs to receive their medication in different packaging, such as a Monitored Dosage System, ALWAYS provide a copy of the package leaflet and a Patient Card, and ALWAYS add a valproate warning sticker to the outer box.

See the Guide for Healthcare Professionals and Summary of Product Characteristics for further information.

Copies of the valproate pharmacy materials (valproate warning sticker, valproate Patient Guide, valproate HCP Guide, valproate Patient Card and valproate Poster) can be ordered from Sanofi Medical Information on:

0800 035 2525 Or by emailing UK-Medicalinformation@sanofi.com

Copies of the materials can also be downloaded from

www.medicines.org.uk

Enter "valproate" in the search box and then click on "Risk Materials" next to any of the medicines listed.

CALL FOR REPORTING

▼ These medicines are subject to additional monitoring. This will allow quick identification of new safety information. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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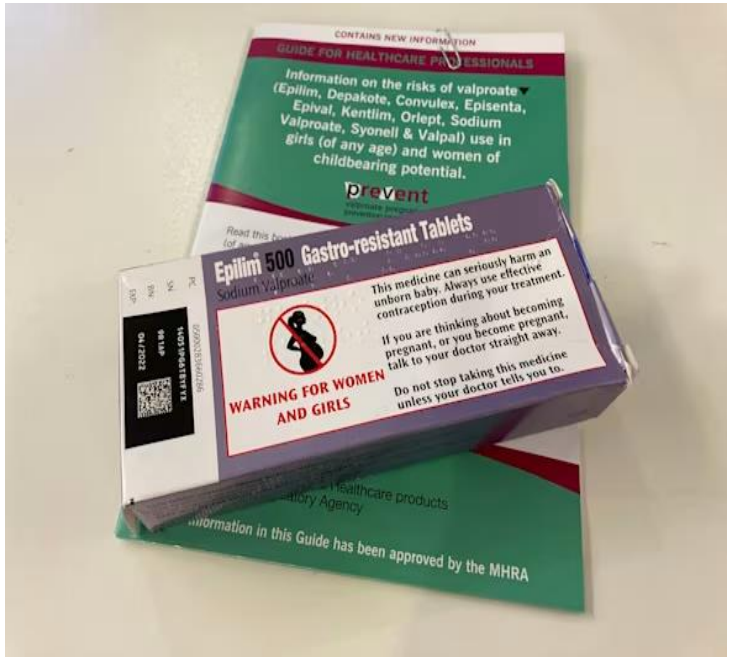
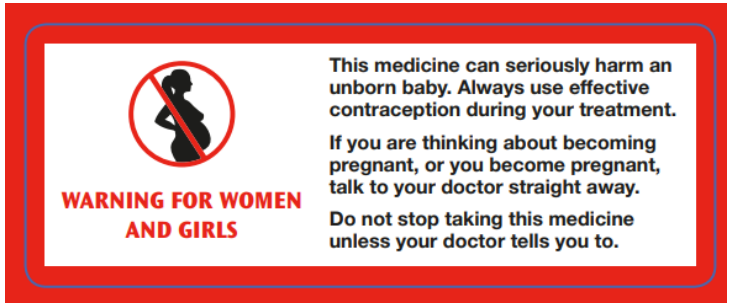
MAT-XU-2305458 (v1.0)

- Ensure women and girls of childbearing potential prescribed valproate are aware of PREVENT and that they are signed up to the PREVENT programme.
- 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; 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.

Actions for community pharmacists

- 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).
- The manufacturer's original full pack does not have to be supplied where:
    - a risk assessment is in place that refers to the need for the patient to be sold or supplied valproate-containing medicines in different packaging from its manufacturer's original full outer packaging (for example, in a monitored dosage system) and
    - assuming that the product is authorised, there are processes in place to make sure that the patient receives the Patient Information Leaflet. That is not the case for unauthorised medicines, unless they are only unauthorised as a result of an assembly process.
- 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).





Referral details for local NHS Providers

Neurology Adults

Organisation	Details
Barts Health NHS Trust*	eRS referral to Neurology services at Newham Hospital, Whipps Cross Hospital and Royal London. You can use Advice & Refer if you need guidance on how to refer.
Barking, Havering and Redbridge University Hospitals NHS Trust (BHURT)	Patients not under the care of BHRUT – GP referral as per usual process Existing Patients under the care of BHRUT – Annual reviews arranged by BHRUT
Homerton Healthcare NHS Foundation Trust	GPs who refer patients who require an ARAF form, which if appropriate, are completed by the responsible specialist clinical team. For established patients, the ARAF is completed during their next relevant follow up appointment.

Referral details for local NHS Providers

Neurology Paediatrics

Children who require an ARAF or RAF for valproate

Place	Details
Barking, Havering and Redbridge	GP referral as per usual process for patients not under the care of BHRUT.
City and Hackney	GPs should refer children to Dr Sanjay Wazir at Homerton Hospital.
Tower Hamlets	GPs should refer children to the Paediatric Neurology team at Royal London Hospital if they are not already under our service
Newham	GPs should refer children to Dr Susan Lieberscheutz at Newham University Hospital
Walthamstow	GPs should refer children to Dr Amit Bali at Whipps Cross Hospital

Referral details for local NHS Providers

Specialist mental health

Organisation	Details
North East London Foundation NHS Trust (NELFT)	GPs will usually refer via the Mental Health and Wellness Teams (MHWT) single point of access. Within NELFT, this is triaged and sent to relevant duty teams to review.
East London Foundation NHS Trust (ELFT)	GPs will usually refer through a Single Point of Entry. Referrals will be processed by the team and may be signposted to other services, or offered an assessment by the team or transferred to a specialist service.

Key messages

For men and boys of childbearing potential consider

- Use the **Valproate Monitoring NEL CEG template**
- Are having a regular treatment review.
- Have a signed Risk Acknowledgement Form (RAF) if newly initiated
- Are aware of the risks of valproate, if taken at conception and to fertility.
- Are using effective contraception and female partner is using contraception during treatment and 3 months after stopping ***as a precaution***
- Have been given the valproate patient guide, or know how to access it online
- Know they must contact their GP if they want to start a family in the next year

For women and girls of childbearing potential consider

- Use the **Valproate Monitoring NEL CEG template**
- Are fulfilling the requirements of a PPP
- Are having an annual review with a specialist.
- Have an up to date, signed, Annual Risk Acknowledgement Form (ARAF)
- Are aware of the risks of valproate, if taken during pregnancy.
- Are using effective contraception.
- Have been given the patient alert card and valproate patient guide or know how to access it online
- Know they must contact their GP urgently for a referral to a specialist if pregnant

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Q&A