NHS
Cornwall and
Isles of Scilly

Prevent inappropriate prescribing of valproate

A system wide approach to reducing inappropriate prescribing of valproate.
January 2024.
Live document: We will review and update this plan accordingly based on new updates and progress.

NHS Cornwall and Isles of Scilly Integrated Care Board

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Action and improvement plan January 2024

Prevent inappropriate prescribing of valproate

Contents

Overview

In November 2023, the Medicines Healthcare Regulatory Agency (MHRA) advised of new regulatory measures for sodium valproate, valproic acid and valproate semisodium to come into force from January 2024. This followed a comprehensive

review of safety data, advice from the Commission on Human Medicines (CHM) and liaison with clinicians and organisations.

Valproate containing medicines are licensed for use in the treatment of epilepsy and bipolar disorder. However, valproate is also used off-label to treat other mental health conditions and migraines.

With the known risk of birth defects and neurodevelopmental disorders following use of valproate in pregnancy, valproate should only be used in women of child-bearing potential if a pregnancy prevention programme (PPP) is in place, which includes a requirement to use highly effective contraception, for patients to be informed of the risks in pregnancy and to have an annual review by a specialist and a signed acknowledgement of risk form (ARAF). Valproate should not be used in female children and women of childbearing potential unless other treatments are ineffective or not tolerated.

Data shows ongoing exposure to valproate in pregnancy despite the current pregnancy prevention programme requirements. Following advice from the CHM on the need for greater scrutiny of the way valproate is prescribed, further new safety measures for valproate-containing medicines are now in place. 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.
C. General practice and pharmacy teams should continue to prescribe and dispense valproate and if required offer patients a referral to a specialist to discuss their treatment options. Valproate should be dispensed in the manufacturer's original full pack.(There will be some exceptions therefore local arrangement or risk assessment needs to be discussed and agreed or completed)
D. Report suspected adverse drug reactions associated with valproate on a Yellow Card.

The valproate safety working group, across the integrated care system (ICS), has been established to coordinate the implementation of the national patient safety alert from November 2023 NatPSA/2023/013/MHRA: Valproate: organisations to prepare for new regulatory measures for oversight of prescribing to new patients and existing female patients.

Benefits of the intervention and impact

- Ensuring people only take valproate in line with the pregnancy prevention programme.
- Reducing harm to babies exposed to sodium valproate in pregnancy.
- Reducing the risk of neurodevelopmental disorders in children whose fathers take valproate in the 3 months before conception.

What success looks like?

- Valproate prescribing only in line with the guidance issued by MHRA and CHM.
- No babies born with birth defects and neurodevelopmental disorders due to inappropriate valproate use.

Reminder of actions for healthcare professionals

Actions for GPs

- Identify and recall all women and girls on valproate who may be of childbearing potential.
- Provide the new updated (December 2023) patient guide to the patient (or her parents or responsible person as necessary).
- Check they have been reviewed by a specialist in the last year (i.e., they have an in-date risk acknowledgement form) and are on highly effective contraception.
- As a precaution, male patients who are planning a family within the next year should speak to a healthcare professional about their treatment options

Actions for specialists

- Have a system in place, to include a second signatory and communicate this, such that review appointments can be booked at least annually with women and girls under the pregnancy prevention programme and re-evaluate treatment as necessary.
- Clearly explain the conditions as outlined in the supporting materials.
- Complete and sign with the patient or their responsible person the risk acknowledgement form—copies of the form must be given to the patient or responsible person and sent to their GP.
- As a precaution, male patients who are planning a family within the next year should speak to a healthcare professional about their treatment options.

Actions for dispensers

- Valproate medicines must always be dispensed with the accompanying patient information leaflet.
- Ensure that patient card is provided every time valproate is dispensed to a female patient.
- Dispense whole packs whenever possible and ensure there is a warning label either on the carton or added via a sticker.

- Discuss risks in pregnancy with female patients each time you dispense valproate medicines and ensure they have the patient guide and have seen their GP or specialist to discuss their treatment and the need for contraception. As a precaution, male patients who are planning a family within the next year should speak to a healthcare professional about their treatment options.
- Ensure new packs of valproate information materials are placed in a designated place accessible to all dispensing staff and dispose of any old materials related to valproate medicines.

New safety and educational materials for patients and healthcare professionals are now available to support the implementation of these measures. These materials can also be found on the eMC website and on the MHRA's valproate safety measures collection page.

- **Updated patient guide:** Provides those taking valproate (or their parent, caregiver, or responsible person) with information on the risks of valproate in pregnancy and the risks to male patients and what they need to do.
- **Updated 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 points for patient discussions.
- **Updated annual risk acknowledgement form:** For female patients starting valproate and at annual review. Used to support and record the discussion between the patient and specialist prescriber on the risks associated with valproate in pregnancy and to record the decision of the countersigning specialist. At subsequent annual reviews only one specialist is required.
- **New 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 males when starting treatment with valproate and to record the decision of the countersigning specialist. This is only to be completed at initiation of valproate.
- **Patient card:** Provides key information for female patients receiving valproate on contraception and pregnancy prevention.
- **Pharmacy poster:** Provides important actions for pharmacists dispensing valproate to female patients.
- **Warning stickers:** To be added to packaging of medicine in exceptional circumstances where the original pack cannot be dispensed.

We ask clinicians to use appropriate individualised language when discussing the implications of taking valproate with patients and their caregivers.

The safety and educational materials should be used alongside other resources to support patients making decisions about valproate and other treatments for epilepsy and bipolar disorder. These include patient support tools, such as those published by the NHS and guidelines produced by the Association of British Neurologists.

Actions required by the national patient safety alert

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:

The Cornwall and the Isles of Scilly integrated care board chief medical officer is the designated executive who will have oversight of the governance systems to ensure that the required actions have been fully completed before actions are recorded as 'action completed'

A. Marco Motta, interim head of prescribing and medicines optimisation ICB, has been appointed chair with delegated responsibility for the actions in this alert.
B. Dr Chris Reid, chief medical officer ICB, executive lead
C. Iain Davidson, chief pharmacist RCHT, and Mike Wilcock, head of prescribing support unit RCHT will link with neurology and paediatric team
D. Helen Woods, chief pharmacist CFT, and Luft Barrat, deputy chief pharmacist CFT, will link with psychiatry and learning disability team
E. Kirsty Lewis, acting director primary care ICB, will link with LMC and GP practices
F. Nick Kaye, CEO community pharmacy Cornwall, and Drew Creek, COO community pharmacy Cornwall, will link with community pharmacies.
G. Lisa Nightingale, head of clinical and quality, patient safety specialist ICB, will link with commissioning teams, local maternity, and neonatal system (LMNS) and Brook.
H. Sarah Dyer, patient safety partner ICB, and Lucy Tuson director of engagement, will link with patients and lived experiences.

The group should be tasked with, and document, progress towards 5 elements:

1. 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.

Action requested of CFT

Review and update shared care guidelines and clinical guidance in line with new regulations and advice. *This action will be delivered through the medicines committee, the specific timeline is detailed within the CIoS valproate safety working group action plan.*

RCHT and CFT are also asked to confirm a process is in place for the two-specialist signatory for new patients (male and female) younger than 55 years.
What kind of request process each system is putting in place for this prescribing/authorisation? *Please confirm the process or proposal of this independent specialist review pathway and governance implication by 31 March 2024.*

RCHT and CFT are asked to confirm process for referrals for review with specialist, and arrangements for ongoing yearly recalls. This information will need to be available on RMS for primary care practitioners. *Please confirm the process by 31 March 2024.*

Action requested of RCHT

Review and update clinical guidance in line with new regulations and advice. *This action will be delivered through the medicines committee, the specific timeline is detailed within the CIoS valproate safety working group action plan.*

RCHT and CFT are also asked to confirm a process is in place for the two-specialist signatory for new patients (male and female) younger than 55 years.
What kind of request process each system is putting in place for this prescribing/authorisation? *Please confirm the process or proposal of this independent specialist review pathway and governance implication by 31 March 2024.*

RCHT and CFT are asked to confirm process for referrals for review with specialist, and arrangements for ongoing yearly recalls. This information will need to be available on RMS for primary care practitioners. *Please confirm the process by 31 March 2024.*

Action requested of ICB

Review and update the formulary in line with new regulations and advice. *Please confirm the review by 31 March 2024.*

2. Commissioning work if necessary to understand the needs of the affected population, including those people most at risk of health inequalities.

Action requested of Lisa Nightingale

Review the joint strategic needs assessment for L/D from public health England. *Please confirm the review by 31 March 2024*.

3. Reviewing the results of local audit(s) of compliance with the existing PPP measures for girls and women of childbearing potential prescribed valproate.

Action requested of ICB, RCHT, CFT and GP practices

ICB to create instructions and a template to be sent to practices to capture current valproate prescribing. Anonymised data will be returned to the ICB prescribing team who will provide details of patient numbers to secondary care. *Please confirm by 31 March 2024.*

CIoS ICB to work with Devon ICB for Devon Trusts. *Please confirm the engagement and further plan by 31 March 2024.*

4. Commissioning/determining the local pathways of care for women of childbearing potential and girls in relation to the prescribing and review of valproate.

Action requested of Lisa Nightingale

Link with the local maternity and neonatal system (LMNS) and Brook. *Please share the outcome by 31 March 2024.*

5. Planning for and identification of clinical resource to meet the identified needs of the population and implement the new regulatory measures.

Action requested of ICB

Identify already available national resources if needed.
Identify patients who potentially might need resources in languages different than what currently available through the MHRA/GOV link.

Action requested of all GP practices

The CIoS valproate safety working group is asking all GP Practices to review their prescribing of valproate in women of childbearing age, and to return the outcomes to the prescribing team. The prescribing team ICB will issue instructions and provide a template to fill out and return.

GP practices are also asked to confirm the following actions *by 31 March 2024*:

- Practice can demonstrate an appropriate 6 monthly search of the clinical system to identify all girls or women of childbearing potential who are also prescribed valproate medicine.
- Confirm all female patients, of child-bearing age AND being prescribed a valproate medicine have a clear indication, e.g., epilepsy, bipolar disorder, migraine etc. for the valproate and this is LINKED to the repeat prescription.
- Confirm all female patients of child-bearing age AND being prescribed a valproate medicine have had a risk assessment completed, by a specialist, in the past 12 months. A copy of this risk assessment is appropriately coded in the notes
- Confirm all female patients of child-bearing age AND being prescribed a valproate medicine have received appropriate patient information leaflets - https://www.gov.uk/guidance/valproate-use-by-women-and-girls#patient-information-leaflets and this is documented in the clinical record E.g. System One – 'Advice on risk harm to foetus from maternal Sodium Valproate during pregnancy' (Y1b25) or 'Advice on risks of harm to fetus from maternal medication during pregnancy' – SNOMED code – 889901000000108. Further codes for use in clinical systems are available in the Q&A document at the bottom of this document.
- Confirm the practice has a robust process in place to ensure that all female patients of child-bearing age prescribed a valproate medicine receive an annual review – as per the pregnancy prevention programme.
- Confirm all females of childbearing potential on valproate are on highly effective contraception, where appropriate, and if not, what should happen? More information on effective contraception is available below.

- Practice can demonstrate an appropriate repeated monthly search of the clinical system to identify all girls or women of childbearing potential who have been recommended to start valproate medication have had a clinical review to ensure compliance with the pregnancy prevention programme as recommended by the MHRA.
- Inform your local medicines optimisation team if there any barriers encountered as part of the valproate pregnancy prevention programme e.g. in communications with specialists. The medicines management teams are working with provider organisations to ensure reviews are carried out by the most appropriate clinician in the most appropriate setting.
- Inform your local medicine optimisation team whether you use the Ardens template to support the safe prescribing and reviewing of patients on valproate, or should you not use Ardens detail what process you have in place.

Ardens Template - GP practice systems

Most GP Practices in CIoS use Ardens:
Ardens has useful tools relating to valproate:

- Pop-up alert
- Monitoring template
- Reports
- Status alert

However, practices who don't use Ardens, need to have a process through EMIS and TPP/S1, or others, to safely prescribing and reviewing patients on Valproate in accordance with current national guidance.

Action for ICB

Audit to be undertaken to understand which practices use Ardens and are successfully using the tool, and which practices do not have Ardens have an agreed process. As above.

Effective Contraception

For more info:

- MHRA issues guidance on contraception for women taking medicines that might increase risk of birth defects - Faculty of Sexual and Reproductive Healthcare (fsrh.org)
- FSRH CEU Statement: Contraception for women using known teratogenic drugs or drugs with potential teratogenic effects (February 2018) - Faculty of Sexual and Reproductive Healthcare

- Effective contraception is essential while taking valproate. At least one highly effective method of contraception, or two complementary forms of contraception including a barrier method, should be used.
- Highly effective contraception is considered for regulatory purposes to be those user independent methods such as the long-acting reversible contraceptives, copper intrauterine device, levonorgestrel intrauterine system, progestogen only implant and female sterilisation, all of which have a failure rate of less than 1% with typical use. Progestogen-only injections have a typical-use failure rate of 6%, but this may be due to repeat injections being administered late. Progestogen-only injections may be considered as highly effective only if repeat injections are documented as having been administered on schedule by a healthcare professional.
- User dependent methods such as the condom, cap, diaphragm, combined oral contraceptive pill or progestogen-only contraceptive pill and fertility awareness based methods are not considered highly effective, since their typical use incorporates user failure risks.

Actions requested of Dispensing Doctors and Community pharmacies

- Valproate medicines must always be dispensed with the accompanying patient information leaflet.
- Ensure that patient card is provided every time valproate is dispensed to a female patient.
- Dispense whole packs whenever possible, and ensure there is a warning label either on the carton or added via a sticker.
- Discuss risks in pregnancy with female patients each time you dispense valproate medicines and ensure they have the Patient Guide and have seen their GP or specialist to discuss their treatment and the need for contraception.
- Ensure new packs of valproate information materials are placed in a designated place accessible to all dispensing staff and dispose of any old materials related to valproate medicines.
- Further supplies of information materials may be obtained: https://www.gov.uk/guidance/valproate-use-by-women-and-girls#patient-information-leaflets

Action requested of RCHT and CFT

The CIoS valproate safety working group is asking RCHT and CFT to review the prescribing of valproate in women of childbearing age. The prescribing team ICB will share their data intelligence based on prescribing from primary care.

Both RCHT and CFT needs to confirm and comment on those figures by their valproate safety working group's contacts *by 31 March 2024*.

Communication and Governance arrangements

The approved plan will be communicated through:

1. The collaborative board
2. The area prescribing committee
3. Local maternity and neonatal system (LMNS) board and the RCHT maternity and neonatal safety champions meeting.
4. Director of engagement for public awareness
5. Public health
6. CFT/RCHT quality assurance committee
7. primary care operational group medical

The approved plan will be monitored monthly through the CIoS valproate safety working group, who will provide an update to the quality assurance meeting (QAM) to include:

- Completed actions. Please note actions may only be recorded as completed with authorisation from the designated member of the executive team.
- Where there is a risk that actions will not be completed by the required deadline
- Where there are outstanding safety alert actions which have passed the deadline for completion.
- Items that require onward reporting/escalation to Quality pathways of care committee (QPOCC), minimum 6 monthly.

Valproate questions and answers

A list of questions and answers compiled on behalf of members of the Valproate Integrated Quality Programme in response to the November 2023 MHRA Alert can be found on the joint formulary. Please note that this document has been shared by NHSE, but is not an official NHSE publication.