



Humber and North Yorkshire
Health and Care Partnership



**Humber and
North Yorkshire**
Integrated Pharmacy and
Medicines Optimisation Committee

Reducing Inappropriate Prescribing of Valproate

Prescribing Focus

A system wide approach to
reducing inappropriate
prescribing of valproate.
May 2023.

ICS Medicines Quality and Safety Group



Prescribing Focus – May 2023

Reducing Inappropriate Prescribing of Valproate

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Overview

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 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. 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 Commission on Human Medicines (CHM) on the need for greater scrutiny of the way valproate is prescribed, further new safety measures for valproate-containing medicines are to be put in place. The CHM has advised that no patient (male or female) under the age of 55 should be initiated on valproate unless two specialists independently consider and document that there is no other effective or tolerated treatment. Where possible, existing patients should be switched to another treatment unless two specialists independently consider and document that there is no other effective or tolerated treatment or the risks do not apply. Further information on how the CHM recommendations will be put into practice is expected. When this is known, this may change the scope, recommendations and metrics/monitoring for valproate accordingly.

The clinically-led Valproate Safety Implementation Group (VSIG) has been established to coordinate a programme of work to reduce the use of valproate in people who can get pregnant by 50% by 2023, and to help prevent unplanned pregnancies in this group of 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.



What success looks like?

- Valproate prescribing **only** in line with the guidance issued by MHRA and CHM.
- Reduction in babies born with birth defects and neurodevelopmental disorders.
- The clinically-led Valproate Safety Implementation Group (VSIG) has been established to coordinate a programme of work to reduce the use of valproate in people who can get pregnant by 50% by 2023, and to help prevent unplanned pregnancies in this group of patients. ([NHS England » Sodium valproate](#))

National Shared Care Protocol

In March 2023, both North Yorkshire and York Area Prescribing Committee and Humber Area Prescribing Committee agreed to adopt the national shared care protocol: Valproate Medicines for Patients on Child Bearing Potential – see link: <https://humberandnorthyorkshire.org.uk/imoc/shared-care-guidelines/>

PLEASE NOTE: This shared care protocol DOES NOT consider the [MHRA statement released in December 2022](#) regarding new safety measures for the initiation of valproate medicines. The national advice and national shared care protocol will be updated in due course, and we are advised to follow the existing precautions, as set out in this shared care protocol.

All providers within Humber and North Yorkshire ICS were given the opportunity, via a 6-week consultation process, to comment on the implementation of the adoption of the national shared protocol (version 1, July 2022). Overall, providers were in favour of adopting and implementing this shared care protocol.

This protocol has been produced to support all prescribers who enter into shared responsibility arrangements to effectively manage the high risk of severe harm from valproate use.

This shared care protocol includes all information required to support safe prescribing in strict accordance with current guidance.



Action Required For All GP Practices

The Humber and North Yorkshire ICS Medicines Quality and Safety Group is asking all GP Practices to review their prescribing of valproate in women of childbearing age, as part of the Valproate Pregnancy Prevention Programme.

All GP Practices are requested to complete the [online form](#) regarding the prescribing of valproate. Even if currently, you have no patients that this applies to.

<https://forms.office.com/r/6hrdWrYSjL>

Please complete the online form by 31st July 2023.

The form asks practices to confirm the following actions:

- Practice can demonstrate an appropriate repeated 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 in the notes AND this is READ coded in the notes – S1 READ code 'Y362e' 'Valproate annual risk acknowledgement form completed'. SNOMED code - Valproate Annual Risk Acknowledgement Form completed - SCTID: 1366401000000107
- *A specialist will not always be required, e.g. if initiated in primary care for migraine. Review on a case by case basis. Use Advice and Guidance, where appropriate. Contact medicines management team if unsure who should complete the review.
- 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

- 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, a clear reason is recorded in the notes.
- 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, via the email address below and or using the form, 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 us if you have implemented any measures for other anti-epileptics (as per . [Antiepileptic drugs: review of safety of use during pregnancy - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/consultations/antiepileptic-drugs-review-of-safety-of-use-during-pregnancy) and if you'd be willing to share best practice.

Ardens Template

We believe most GP Practices in Humber and North Yorkshire use Ardens.

Ardens has useful tools relating to valproate:

<https://support.ardens.org.uk/support/solutions/articles/31000142862-valproate>

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



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.

Metrics and monitoring

NHS BSA ePACT2 has [The Valproate Safety Dashboard](#) – individual practices can look at their own most recent data.

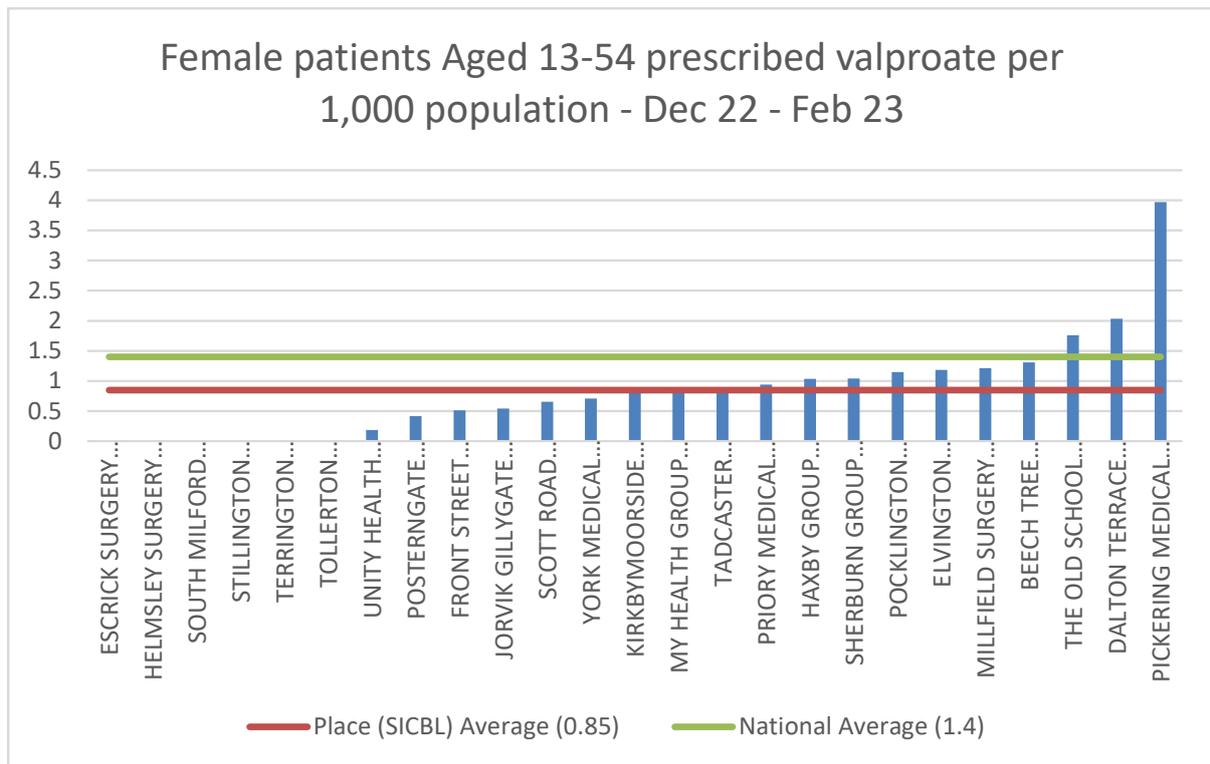
<https://digital.nhs.uk/data-and-information/publications/statistical/mi-medicines-and-pregnancy-registry>



Local prescribing data – Humber and North Yorkshire ICS

Female patients Aged 13-54 prescribed valproate per 1,000 population - Dec 22
- Feb 23

York Health and Care Partnership (Place/SICBL)



Actions for Dispensing Doctors Only

(separate comms will be sent to Community Pharmacies)

- Valproate medicines must always be dispensed with the accompanying patient information leaflet
- 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>

System Wide Approach

We are working with other stakeholders e.g. mental health providers, acute trusts and community pharmacies, to ensure all parts of the system support response required for the valproate pregnancy prevention programme.

If a practice has any issues with implementing any of the above recommendations please contact the relevant Place medicines optimisation teams to identify and escalate the issues.

North Yorkshire AND York GP Practices: hnyicb-ny.rxline@nhs.net

Please DO NOT send any patient identifiable data via this form or via email. The medicines optimisation team will request information if needed, in line with data governance processes.

Please note that all practices (including those who currently have no patients to whom this applies) need to complete the online survey.

Please ensure you have responded by 31st July 2023.

Yours sincerely,

Humber and North Yorkshire Medicines Quality and Safety Group

Why This Matters

Valproate use in pregnancy is associated with an increased risk of children with congenital abnormalities and developmental delay. Valproate is contraindicated in women of childbearing potential unless the conditions of the valproate pregnancy prevention programme are fulfilled.



Whilst the rates of prescribing of valproate continue to decline slowly there are wide geographical variations in prescribing. Clear actions have been set for general practices to identify and recall existing patients, provide them with a copy of the Patient Guide, to check they have had a specialist review in the last year and to have systems in place to identify and appropriately manage new patients who are prescribed valproate and are of child-bearing potential.

The pregnancy prevention programme requires GPs to:

- Ensure continuous use of highly effective contraception* in all women of childbearing potential (consider the need for pregnancy testing if not a highly effective method).
- Check that all patients have an up to date, signed, Annual Risk Acknowledgment Form each time a repeat prescription is issued.
- Ensure the patient is referred back to the specialist for review, annually.
- Refer back to the specialist urgently (within days) in case of unplanned pregnancy; or
- where a patient wants to plan a pregnancy.

Further Information

- We have a wide-range of resources and information on our website:

<https://humberandnorthyorkshire.org.uk/imoc/medicine-safety/>

Please click on 'sodium valproate' to open the links.

- For full guidance from MHRA please see:
<https://www.gov.uk/guidance/valproate-use-by-women-and-girls>
- Drug safety update (MHRA) - Valproate: reminder of current Pregnancy Prevention Programme requirements; information on new safety measures to be introduced in the coming months.
- Sodium Valproate resources and information | General Pharmaceutical Council (pharmacyregulation.org)



- Good practice: [Considering Valproate \(yourhealth.tv\) video](#)

Case studies and examples of good practice

- [Discussing the risks of sodium valproate - ethical learning material - GMC \(gmc-uk.org\)](#)
- <https://www.rcpch.ac.uk/resources/valproate-use-women-girls-childbearing-years-guidance>
- Ensuring patients only take valproate in line with the [Pregnancy Prevention Programme](#)

Valproate - A timeline & Further Info and Resources

January 2015, the Medicines and Healthcare products Regulatory Agency (MHRA) issued a drug safety update highlighting the risks associated with sodium valproate

2018 - the MHRA said that valproate must not be prescribed to women or girls of childbearing age, unless they are on a pregnancy prevention programme (PPP). Guidance states that any woman prescribed the drug should also receive a patient alert card that warns them of the dangers of taking the drug while pregnant.

During 2018, all practices and individual GPs will have been sent a pack of information advising them of the need to identify any girl or woman of childbearing potential (this is defined as a pre-menopausal woman who is capable of becoming pregnant) currently being prescribed valproate and setting out a series of actions for health professionals including GPs.

In 2019, the MHRA strengthened regulations governing its use: the pregnancy prevention programme, PPP, is a key element of these regulations.

March 2019, updated January 2021 - Thirteen UK healthcare bodies launch 'pragmatic' guidance on valproate use -

<https://www.rcpch.ac.uk/news-events/news/thirteen-uk-healthcare-bodies-launch-pragmatic-guidance-valproate-use>



April 2019 - GMS Contract/QOF guidance

<https://www.england.nhs.uk/wp-content/uploads/2019/05/gms-contract-qof-guidance-april-2019.pdf>

Prescribing Safely/Quality Improvement Module:

All practices should undertake an audit of the current quality of their prescribing in relation to the following measures:

Girls and women of childbearing potential currently being prescribed valproate have had an annual specialist medication review and are taking this in compliance with the pregnancy prevention programme as documented by a specialist in the annual risk acknowledgement form. This standard applies to unlicensed use for pain, migraine and other conditions.

Even if a practice does not have any girls of any age or women of childbearing potential who are currently prescribed valproate, they should ensure their practice has a robust system in place to identify and refer for annual specialist review any new at-risk patients being prescribed valproate and should ensure continuous measurement of this measure. The inclusion of valproate prescribing and monitoring seeks to further promote health care professional awareness of the appropriate monitoring actions whilst awaiting the report of the Independent Medicines and Medical Devices Safety Review, chaired by Baroness Cumberlege.

An audit function is available on all GP software systems to identify and recall all women and girls being prescribed valproate who may be of child bearing potential. Contractors should use this tool in preference to developing their own bespoke searches.

There is a prescribing safely audit tool available for sodium valproate which may be useful - [Appendix-e-iii-template-for-qof-prescribing-safety-module-sodium-valproate-v10-docx.docx](#) (will need to log-in via NHS mail to access)

8 July 2020 - The Independent Medicines and Medical Devices Safety Review, chaired by Baroness Julia Cumberlege, published its report - [“First Do No Harm”](#) This included a full section on sodium valproate use in pregnancy – section 4. This report found that women were still becoming pregnant while taking valproate, without



any knowledge of the risks. It estimated that hundreds of babies were being born each year after being exposed to valproate *in utero*, despite the teratogenic risk being well recognised.

Jan 2021 – MHRA extends its review to all antiepileptics [Antiepileptic drugs: review of safety of use during pregnancy - GOV.UK \(www.gov.uk\)](#)

2021, [NHS England set a target of reducing the use of valproate in people who can get pregnant by 50% by 2023.](#)

April 2022, [NHS Digital published figures](#) showing that 949 women in England on the valproate register have had a pregnancy since April 2018, 247 (26%) of whom were prescribed sodium valproate during their pregnancy.

Of these, 46 women were prescribed sodium valproate during their pregnancy in the most recent recording period, from October 2020 to September 2021.

16th April 2022 – Sunday Times published 'A scandal worse than thalidomide' - <https://www.thetimes.co.uk/article/the-new-thalidomide-d5lmlwvdc> (need to sign-up for a free trial to access the full article)

Responding to a Sunday Times investigation, published today, on continued use of sodium valproate for women of child-bearing age, Professor Martin Marshall, Chair of the Royal College of GPs, said:

"The use of sodium valproate is strictly regulated given the terrible effects it can have on the children born to women taking it during pregnancy. It should not be prescribed to women of child-bearing age unless they are on a pregnancy prevention plan or there are exceptional circumstances."

19th April 2022 – other antiepileptics - [MHRA publishes guidance on pregabalin and risks in pregnancy](#)

May 2022 - The Medicines and Healthcare products Regulatory Agency (MHRA) has launched a review into safety issues around sodium valproate prescribing and is seeking views of patients and healthcare professionals in advance of a meeting of the Commission on Human Medicines. -

<https://www.gov.uk/government/organisations/commission-on-human-medicines/about/membership#sodium-valproate-expert-working-group>

July 2022 – National shared care protocol published – the version that Humber and North Yorkshire have adopted.



December 2022 - [MHRA statement released in December 2022](#) regarding new safety measures for the initiation of valproate medicines. The national advice and national shared care protocol will be updated in due course, and we are advised to follow the existing precautions, as set out in this shared care protocol.