For Collaboration Purposes

Valproate Q&A

Q&A in response to questions arising following the publication of the National Patient Safety Alert issues by MHRA November 2023

Q	How can I be part of the national Valproate Integrated Quality Improvement Programme?
A	Join the collaboration space at Medicines Safety Improvement Programme - FutureNHS Collaboration Platform. Request invites to group meetings and workshops at england.medicinessafetyimprovementprogramme@nhs.net
Q	When and where will the new supporting materials like the new ARAF, RAF for men, patient card and leaflet and healthcare professional information be available?
A	These are available at Epilim 200 mg Gastro-resistant tablets - Risk Management Materials - (emc) (medicines.org.uk) and Valproate safety measures - GOV.UK (www.gov.uk)
Q	The new ARAF for women and RAF for men are editable PDFs. Does it still need a wet signature?
A	No. Wet signatures are not required by initiating specialist, countersigning specialist nor patient/parent/carer.
Q	How will we confirm that people are on a suitable contraceptive and that they remain on it?
A	There will need to be local arrangements for this. Please contribute any examples to england.medicinessafetyimprovementprogramme@nhs.net for sharing on Medicines Safety Improvement Programme - FutureNHS Collaboration Platform.
Q	What is considered “highly effective” contraception?
A	The SPC states “At least one effective method of contraception (preferably a user independent form such as an intra-uterine device or implant) or two complementary forms of contraception including a barrier method should be used. Individual circumstances should be evaluated in each case, when choosing the contraception method involving the patient in the discussion, to guarantee her engagement and compliance with the chosen measures.” The terms “highly effective” and “user independent” can be used interchangeably.

Compiled by Tony Jamieson on behalf of members of the Valproate Integrated Quality Programme.
Updated 1st Feb 2024

	The decision support tools can be used to help patients consider which forms of contraception provide them with the highest acceptable protection. NHS England » Decision support tool: bipolar disorder – is valproate the right treatment for me NHS England » Decision support tool: is valproate the right epilepsy treatment for me? See also Faculty of Sexual and Reproductive Health guidance at: https://www.fsrh.org/standards-and-guidance/documents/fsrh-ceu-statementcontraception-for-women-using-known/teratogenic-medication-and-contraceptionfsrh-ceu-statement-february-2018.pdf The additional protective effect of using barrier method with oral contraception has not been quantified in the guidance and is not considered to be as effective as a user-independent method.
Q	Can the ARAF form reflect that sometimes a patient will have no other option but to be on Valproate while they are pregnant – i.e., make a risk-based decision.
A	In the exceptional circumstances that a patient chooses to continue with Valproate (or start Valproate) whilst they are pregnant it is advisable to have a detailed local consent documentation and detailed care records. The use of Valproate in pregnancy is contraindicated other than for patients with epilepsy where there is no other effective or tolerated treatment.
Q	In a pre-menarche patient there are 2 specialists when we start treatment. Are we expecting an ARAF to be completed each year?
A	Female patients do not require an ARAF between initiation and onset of menarche. How long to leave patients without a clinical review of their condition is a separate issue. ICBs may also wish to consider how comfortable that are for the onus to be on the patient's parent/carer to remember to act at the onset of menarche, particularly for the most vulnerable and least activated patients and families. A onesize-fits all approach is unlikely to be sufficiently reliable.
Q	Will the National Shared Care Protocol be updated?

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	No. In its place, members of the Valproate Integrated Quality Improvement Programme are producing a template to help Integrated Care Boards define their local organisational and professional roles and responsibilities. This will be available at: Medicines Safety Improvement Programme - FutureNHS Collaboration Platform and is expected by the end of February 2024. Guidance on Valproate use in women and girls of childbearing years is available to consider roles and responsibilities, although it is not updated to include the role of countersigning specialists: Pan_College_Guidance_Document_on_Valproate_Use_V2.1__26_Jan_Update.pdf (publishing.service.gov.uk)

	CQC valproate high risk medicine
Q	Does the countersigning specialist have to be a prescriber?
A	The regulatory measures do not require the countersigning specialist to be a prescriber. As a precautionary measure, until such time as legal precedent is set on individual accountabilities (for initiating specialist and countersigning specialist), having the legal authority to prescribe may provide a level of assurance of parity between specialists. The CHM recommends that the countersigning specialist offers "an appropriate level of **increased** clinical oversight of valproate prescribing". Employers and Integrated Care Boards must be assured that countersigning specialists can offer an appropriate level of increased clinical oversight. The Association of British Neurologists and British Paediatric Neurology Association have produced guidance that goes further than the MHRA in defining both initiating and countersigning specialist.
Q	What constitutes an adequate MDT?
A	If the lead of the MDT is to act as the independent countersigning specialist, then the MDT should include people with sufficient knowledge, skills and influence to provide "**increased** clinical oversight". A toolkit to support the formation of an MDT can be found here: MDT Toolkit(hee.nhs.uk)
Q	Can prescribing software providers be influenced nationally to work with NHS hospitals and GP practices to put systems in place that support Valproate safety?
A	NHS England does not have the powers to mandate system suppliers to take action. However, the situation can be brought to their attention and highlighted as a safety issue.

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Q	Will there be a national patient-identifiable registry for recording the acknowledgement of risk (ARAF) and Pregnancy Prevention Programme (PPP) information? Perhaps something like Pathfinder for Lenalidomide or the system for Clozapine?
	Not in the short to medium term. Discussions have been held and there are some considerations relating to Pathfinder that could be extended to any national standalone data repository/register. The differences with Valproate are: • The limited number of Lenalidomide patients compared to over one hundred thousand Valproate patients under the age of 55. • The very limited number of Lenalidomide prescribers compared to over eight thousand GP practices.
	• The very limited number of pharmacies supplying Lenalidomide compared to the 11,000+ community pharmacies. • Pathfinder monitors stock movement so that no supply can be made by wholesalers unless there is a named patient and accompanying signed risk form. For Valproate there are no controls on supply (and should not be) therefore there is no physical barrier to supply without using Pathfinder/the register. • Pathfinder is used exclusively by secondary care, and manufacturers may not supply unless it is used. Requiring general practice and community pharmacy to use Pathfinder would require contractual changes that would be subject to national funding and negotiation with both BMA and CPE. • Each prescriber and supplier (including locums) would need their own unique log-in and password and potentially training to use the system. • Pathfinder does not have interoperability with primary care nor secondary care software systems and therefore requires double entry. It has however worked for lenalidomide with zero exposed pregnancies so far.
Q	How can we improve coding and transfer of coded data between providers?
A	A list of the existing Read and Snomed codes has been produced by North East and North Cumbria Integrated Care Board. All ICBs might consider using these codes in the same way. In general practice it is helpful to have the indication(s) linked to the prescribing of valproate. In addition, there are a range of codes to describe the biological exemptions from the Pregnancy Prevention Programme (such as Hysterectomy), code for the insertion of or presence of IUD/S or implant. Discussions are taking place with the Summary Care Record Team and NHS App Team to explore how these coded entries can be made available to all the providers that need to see them.

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Q	Is there patient Information which supports patient with learning difficulties either pictorial or in easy read form or languages other than English?
A	There are examples of easy-read documents available at: https://future.nhs.uk/MedicinesSafetyImprovement/view?objectId=48707088 There is a pressing unmet need for more accessible resources. Please contribute any examples to england.medicinessafetyimprovementprogramme@nhs.net for sharing on Medicines Safety Improvement Programme - FutureNHS Collaboration Platform.
Q	Is there a national audit tool or link to the National Audit Program to mandate Trusts to undertake and assign resources to provide consistency?
A	The below two national audits exist and can be helpful in considering the quality of care for adults with epilepsy and those with bipolar at: Prescribing Observatory for Mental Health (POMH) | Royal College of Psychiatrists (rcpsych.ac.uk)

	NCEPOD: Disordered Activity? (epilepsy care for adults) – HQIP These are not mandated nationally; however, integrated Care Boards and providers may choose to engage for the purposes of self-assessment and benchmarking to inform their Action and Improvement Plans. For children and young people, the below audit provided by RCPCH is mandated for providers as part of the National Clinical Audit and Patient Outcomes Programme: Epilepsy12 audit | RCPCH Many Integrated Care Boards (and formerly Clinical Commissioning Groups) have conducted audits in primary care of the reliability of the Pregnancy Prevention Programme. Examples are available at: Medicines Safety Improvement Programme - FutureNHS Collaboration Platform.
Q	Should action be taken for men prescribed Valproate?
A *	Please see the September 2024 drug safety update Valproate use in men: as a precaution, men and their partners should use effective contraception - GOV.UK • This question and answer have been updated by CIOSICB Jan 2025 after the updated guidance was released in Sep 2024. Permission was given by Tony Jamieson to amend the document.
Q	Will the decision support tools be updated?

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A	The new regulatory measures do not change how the risks and benefits of Valproate should be described or discussed with patients. There are no new risks for women with childbearing potential. As such there is no requirement to change the published decision support tools available at: NHS England » Decision support tool: bipolar disorder – is valproate the right treatment for me and NHS England » Decision support tool: is valproate the right epilepsy treatment for me? Decision support tools for other patient groups are needed. Please contribute examples to england.medicinessafetyimprovementprogramme@nhs.net for sharing on Medicines Safety Improvement Programme - FutureNHS Collaboration Platform.

Q	Is there advice on the management of patients from abroad or transferring from the independent sector?
A	The regulatory requirements apply to all patients being prescribed or considering being prescribed Valproate, irrespective of whether they are NHS patients, private patients or patients from abroad receiving care in England and apply in all circumstances when the NHS delivers care. As such local policies, processes and pathways need to accommodate patients as they enter and leave NHS care.
Q	How is menopause confirmed in women younger than 55?
A	The likelihood of a natural pregnancy for a woman who is 55 years old is very low. Menopause does not need to be confirmed for women over the age of 55. For women under 55 years old the NICE guidance should be followed at: Recommendations | Menopause: diagnosis and management | Guidance | NICE
Q	Is there going to be national clinical guidance on what treatments must be tried first? (Currently there is prescribing guidance from NICE and guidance from the Maudsley Hospital that are different – mostly due to difference in licensing for certain products, and NICE does not tend to recommend off label products.)
A	NICE clinical guideline CG185 Bipolar disorder: assessment and management has been updated and reflects the MHRA regulatory position. NICE guideline NG217 Epilepsies in children, young people and adults already cross references MHRA guidance. It is not anticipated that there will be guidance that supports the use of Valproate in any unlicensed indications such as migraine.
Q	Do the regulatory requirements apply in for patients with cancer or during palliative care and end of life?

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A	There are no specific exemptions in the regulatory requirements for female patients under the age of 55 who have cancer, or during palliative care or the end of life, other than the phrase “The absence of pregnancy risk is considered to be permanent”. Palliative care can be provided over extended periods of time depending on the condition. For some patients annual review may be more appropriately conducted within the cancer pathway with input from neurology.
Q	Is there going to be national guidance around information sharing?
A	This is being explored, but is in the earliest stages. Please contribute examples to england.medicinessafetyimprovementprogramme@nhs.net for sharing on Medicines Safety Improvement Programme - FutureNHS Collaboration Platform.

Q	Are we going to get national guidance around complete packs and suicide and self-harm risk?
A	Please contribute examples to england.medicinessafetyimprovementprogramme@nhs.net for sharing on Medicines Safety Improvement Programme - FutureNHS Collaboration Platform.
Q	What is known about the needs of the affected population, including those people most at risk of health inequalities?
A	Both epilepsy and bipolar have higher prevalence in populations with higher levels of deprivation. In addition, providers have expressed concern that patients form deprived or under-served communities are at increased risk of having a reduced level of protection from the pregnancy prevention programme. Similar concerns have been raised for patients for whom communication barriers exist either due to language or understanding. And for those with a learning disability or neurodiversity and those with more than one indication for Valproate such as co-existing epilepsy and bipolar. Concerns have been raised that transgender patients are at increased risk, particularly if they have been provided with an NHS number that is not the same as the one issued at birth. Ethnic and religious believes about contraception are also a consideration. Other risk factors have been identified such as children in care, patients with a safeguarding risk management plan, homelessness, new entrants to the UK and asylum seekers.
Q	Where can I find exemplar arrangements with patient representatives / representative groups?

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A	NHS England – South East regional team have plans for engaging patients in codesign work. Please contribute examples to england.medicinessafetyimprovementprogramme@nhs.net for sharing on Medicines Safety Improvement Programme - FutureNHS Collaboration Platform.
Q	What if we don't or can't implement the new regulatory requirements?
A	The new requirements are part of the authorisation for use of valproate and if they are not followed it would be considered off-label prescribing (Off-label or unlicensed use of medicines: prescribers' responsibilities - GOV.UK (www.gov.uk)). On an individual prescriber level this might mean they may not be able to meet the GMC's professional standard expectations, which can be found in both Good Medical Practice and Good Prescribing Practice or equivalent for nonmedical prescribers.
	At a system or provider level, this would fall under the remit of the CQC as the regulator of care. The CQC's Guidance on Safe Care and Treatment 12(2)(b) states: • Providers must do all that is reasonably practicable to mitigate risks. They should follow good practice guidance and must adopt control measures to make sure the risk is as low as is reasonably possible. They should review methods and measures and amended them to address changing practice. • Providers should use risk assessments about the health, safety and welfare of people using their service to make required adjustments. These adjustments may be to premises, equipment, staff training, processes, and practices and can affect any aspect of care and treatment. • Relevant health and safety concerns should be included in people's care and treatment plans/pathways. This includes allergies, contraindications and other limitations relating to the person's needs and abilities. • Staff must follow plans and pathways. • Medication reviews must be part of, and align with, people's care and treatment assessments, plans or pathways and should be completed and reviewed regularly when their medication changes. • Providers must comply with relevant Patient Safety Alerts, recalls and rapid response reports issued from the Medicines and Healthcare products Regulatory Agency (MHRA) and through the Central Alerting System (CAS). CQC's 'safety alert' describes the responsibilities in General Practice. Please contribute examples of provider risk assessments to: england.medicinessafetyimprovementprogramme@nhs.net for sharing on Medicines Safety Improvement Programme - FutureNHS Collaboration Platform.

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Clinical system coding

NHS
North East and North Cumbria

	SystmOne code	SNOMED Concept ID
Pregnancy Prevention Programme started *To be used when an ARAF is received from secondary care and ongoing annual reviews are required*	Y2f16	1129771000000103
Pregnancy Prevention Programme declined *To be used the patient has been referred to secondary care, was given an appointment for ARAF completion but did not attend*	Y2f17	1129801000000100
Pregnancy Prevention Programme not needed *To be used when an ARAF is received from secondary care and ongoing annual reviews are not needed, for example, a patient who is of childbearing age but has had a hysterectomy*	Y2f18	1129791000000104
Pregnancy Prevention Programme discontinued	Y2f19	1129841000000102
Did not attend Pregnancy Prevention Programme	Y2f1a	1129831000000106
Pregnancy Prevention Programme declined by parent	Y2f1b	1129821000000109
Pregnancy Prevention Programme declined caregiver	Y2f1c	1129811000000103
Valproate Annual Risk Acknowledgement Form completed *To be used when Valproate ARAF received from secondary care*	Y362e	1366401000000107
Referral for completion of Valproate Annual Risk Acknowledgement Form *To be used when a referral has been made from primary care to secondary care*	Y38a6	1366381000000107