Valproate Q&A For General Practice

Questions arising following the publication of the Drug Safety Update article on the risk of neurodevelopment disorders in the children born to men or people who can father children who have taken valproate in the 3 months before conception (referred to as 'paternal risk').

NB. Further advice may be provided by royal collages as consensus emerges. Such advice will supersede this document which is published to stimulate debate.

Q1	**Where can I learn more about the paternal risk?**
A	Link to drug safety update webpage: https://www.gov.uk/drug-safety-update/valproate-use-in-men-as-a-precaution-men-and-their-partners-should-use-effective-contraception Detailed background information can be found in the MHRA's public assessment report: https://www.gov.uk/government/publications/valproate-review-of-safety-data-and-expert-advice-on-management-of-risks
Q2	**When and where will the new supporting materials such as the Risk Acknowledgement Form (RAF) for men starting valproate (aged under 55yrs), 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 other brands) and https://www.gov.uk/government/collections/valproate-safety-measures and Advice for male patients on valproate to use contraception and visual risk communication diagram to be used by a healthcare professional when counselling on the risks. There may be a delay between the publication of Drug Safety Update (5th Sept 2024) and the availability of the updated supporting materials from the drug manufacturers
Q3	**The MHRA's publication refers to men and males. Do the risks apply to trans-women who retain the capability to generate sperm.**
A	Yes, the risks apply to anyone who can biologically father children. Practices should consider this when searching their systems for at-risk patients as trans-women may not be included in the search results of male patients.

Compiled by Tony Jamieson, NHSE, on behalf of members of the Valproate Integrated Quality Programme. Updated 29th August 2024. Adopted with permission from NHSE. Approved by BNSSG APMOC December 2024, review December 2027.

Q4	**Is there an age limit for this risk, like there is for women? Continues below**
A	No. However, it remains less common for men over the age of 50 to father children.
Q5	**How should I prioritise which men and trans women I should have a conversation with first:**
A	1. Any patients known to the practice to be in IVF treatment or spontaneously declaring their intention to father children. (It is not expected that practices will be able to systematically identify this group, this information may be provided opportunistically by patients) 2. Patients with a Learning Disability 3. Trans-women with ability to generate sperm 4. Patients with sensory disability, language or communication barriers. 5. Patients with both epilepsy and bipolar disorder. 6. Patients stratified by age, starting with the age group in your community with the highest conception rates. 7. Patients who have had a vasectomy. Cohorts 2 to 4 are prioritised due to the health inequalities experienced by these groups.
Q6	**Do all the men and transgender-women who the practice prescribed valproate to need to have a Risk Acknowledgement Form (RAF) completed?**
A	No. Only men and transgender-women who have been initiated on valproate after the 31st Jan 2024 will have a RAF. This will be completed by the initiating specialist.
Q7	**If a man or transgender-woman has had a RAF completed in the past, does it need to be repeated annually.**
A	No.
Q8	**Does the practice need to have a consultation with all the men or transgender-women to whom they prescribe valproate to tell them about the paternal risks.**
A	**All men and transgender-women** currently taking valproate should be informed about the risk. There is a professional responsibility and failure to inform the patients of the risk may leave the prescriber open to a claim or complaint to the regulators. Practices are able to communicate the risk to patients in any way they feel meets the patient's needs. Electronic messaging is commonplace (example AccuRX messages) and the practice may consider this appropriate for some or all of their patients.

	Practices have suggested a simple signposting message advising that new risks have been found for men and transgender-women who take valproate medicines and father children. Include a link to the patient information and a reminder not to stop taking valproate without discussing it with a healthcare professional. It may be possible for the patient to acknowledge receipt of this information electronically. (Also See Q12 on SNOMED codes)
Q9	**How can I prepare to have a consultation about the paternal risks with a man or transgender-woman who is taking valproate.**
A	Patients have said that their satisfaction with a consultation about valproate improves when: • They have been advised in advance of the subject matter. • The clinician is well informed about the risk. • The clinician is confident and comfortable with the discussion. • The clinician asks what is important for the patient. • The clinician uses language that the patient finds easy to understand. Clinicians should understand the information in the Health Professional Guide produced by the drug manufacturers and may consider simulation training with trusted peers before embarking on the consultations. For pharmacists and pharmacy technicians there is a helpful workshop produced by CPPE; "The Hard Conversations" which may help prepare. (log-in required). A template invite letter and resource to support conversations with people with a learning disability are also available on BNSSG Remedy website.
Q10	**Who, in the practice team, is able to hold a consultation about the paternal risks with a man or transgender-woman who is taking valproate?**
A	Any registered healthcare professional, such as GPs, Pharmacists and Nurses who are confident and competent to complete the consultation.
Q11	**Now that the paternal risks have been identified is there a deadline by which time the practice must have informed all the affected patients?**
A	The MHRA has not set a deadline. Commonly practices have suggested that they will see patients at their next scheduled review following their usual procedures for medication review (or other review of long-term conditions).
Q12	**How should the practice record and code that the patient has been informed about the paternal risks?**
A	For new male patients the practice can record the receipt of the RAF using: 2078961000000109 |Risk Acknowledgement Form for Male Patients Starting Valproate completed (situation)| For existing valproate patients a non-specific SNOMED code is appropriate along with a freetext annotation of 'valproate' and 'Risk of Neurodevelopmental Disorder': 396080005 |Medication side effects education (procedure)|

Q13	**Should all the men and transgender-women to whom the practice prescribes valproate be referred to a specialist.**
A	There is **no requirement to refer patients, as a result of these paternal risks**, **unless the patient has epilepsy or bipolar disorder and wishes to discuss their treatment options.** It is anticipated that discussions about treatment options in epilepsy or bipolar disorder is out-of-scope of practice for majority of primary care clinicians. Practices may wish to use the advice & guidance route before making a referral dependent on local pathways and referral-to-treatment times. Before making a referral, the GP may wish to consider with the patient: • Have other options already been tried? Did they help? • Any barriers to a changing medication. • Severity of disorder and degree of treatment resistance. • Current symptomatology. • Current insight and decision-making capacity. • Adherence to current medication. For unlicensed uses of valproate such as migraine, neuropathic pain and mood stabilisation (other than bipolar disorder), there is less evidence of efficacy and prescribers may wish to consider the justification for continuing therapy.
Q14	**What should I do if a sexually active man or transgender-woman who understands the risks tells me that they will not use contraception or will not ask their partner(s) to use contraception.**
A	The man or transgender-woman's autonomy must be respected. Opportunities should be taken to understand the patient's reasons, dispel any misunderstanding and counsel them on the consequences of their choices whilst offering support to take alternative actions. Clear documentation of the discussion should be made in the notes (see question 12 on records and coding)
Q15	**What should I do if a man or transgender-woman who is taking valproate says that they are planning to father a child and can't wait to see a specialist so will stop taking their valproate?**
A	Advise the patient that their epilepsy or bipolar disorder may deteriorate without valproate, or an alternative medication and that deterioration can be fatal. Discuss that we do not currently know if the neurodevelopmental disorders (NDD) caused by valproate taken by fathers can be distinguished from baseline incidence so stopping valproate is no guarantee of a child without NDD. If the valproate is prescribed for conditions other than epilepsy or bipolar disorder, consider supporting the patient's decision to stop with safety-netting.
	Continues below

Q16	**What should I do if a man or transgender-woman taking valproate expresses concern that their child or children might have been affected.** **What should I do if a woman or transgender-man expresses concern that their child or children might have been affected by the paternal exposure to valproate.**
A	Check if the use of valproate was within 3 months of conception. Discuss the risks have been shown when sperm have been exposed to valproate (at any point in the cycle which produces sperm which is slightly less than 3 months) but the risks have not been studied when valproate was stopped more than 3 months before conception. Advise them of the relative risks and the uncertainty of the causal nature of valproate. We do not currently know if the neurodevelopmental disorders (NDD) caused by valproate taken by fathers can be distinguished from baseline incidence. Explain that NDD can take many forms and in some people this may be diagnosed later in life. Follow local protocols for referral to a specialist for neurodevelopmental disorders if the parents are concerned and the affected person has displayed signs of an NDD. Remedy has information on Special Educational Needs & Disability (SEND) in BNSSG. Parents can be referred to these groups for more help and advice: INFACT - Home – INFACT (infactuk.com) who provide information, advice and support to families. OACS - Organisation for Anti-Convulsant Syndrome | Valproate | Epilim (oacscharity.org) who provide support to all families touched by Fetal Anticonvulsant Syndrome