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 possible risk of testicular toxicity do not apply. All male patients and/or carers should be made aware of the possible risk to children born to men treated with valproate in the 3 months before conception, of the risk of infertility in men and of the data available showing testicular toxicity in animals exposed to valproate and the uncertain clinical relevance.

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, the possible risk of testicular toxicity and the possible risk to offspring.

- 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, Alprolep, Belvo, Convulex, Dyzantil, Episenta, Epival, Syonell & Sodium Valproate (Crescent, Desitin, Strandhaven/Somex, Wockhardt)) – 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.
- This document can be completed electronically, wet signatures are not required.
- If the 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 patient's notes.

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:

Risk minimisation material fulfils the conditions of the marketing authorisation and has been approved by MHRA.

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Step 1: Specialist prescriber and countersigning specialist: Document the prescribing decision

Actions to be completed by the specialist prescriber to confirm the prescribing decision	**Initial to confirm all that apply**
• The patient's condition does not respond adequately to other treatments or other treatments are not tolerated.	
• I have discussed the risks with the patient, and I consider the balance of benefits and risks to be favourable.	
• I have offered the patient a copy of the Patient Guide and they know where to get further information.	
• The risk of infertility, potential risk of testicular toxicity, or potential risk to offspring do not apply for the following reason(s):	

To be completed by the countersigning specialist prescriber (can be completed by specialist prescriber following discussion with countersigning specialist if needed)	**Initial to confirm all that apply**
• Their condition does not respond to other treatments or other treatments are not tolerated.	
• They have been informed of the risks and I consider the balance of benefits and risks to be favourable	

To be completed by the patient if they consider the risks of valproate do not apply to them	
☐ I confirm that I agree the risks of valproate do not apply to me.	
Name of patient:	
Name of responsible person (if applicable):	
Signature of patient (or responsible person):	**Date:**

Patients who have completed the declaration in the box above do not need to complete step 3 on this form.

Step 2: Specialist prescriber: Explain the risks to the patient or responsible person

Information to be discussed with the patient or responsible person	**Initial to confirm you have discussed**
Fertility while on valproate • Valproate may cause infertility in some male patients. This can make it difficult to have a baby. • Male infertility may be reversible after valproate is stopped or after a dose reduction in some patients.	
Effects on male reproductive system • Some studies in male animals have shown valproate to have an adverse effect on parts of the male reproductive system. These include toxic effects on the testes (testicles). • The weight of the developing testes (testicles) was lower in young animals given valproate and it is unclear what this means for humans.	
Potential risks to children born to fathers taking valproate • A retrospective observational study suggests an increased risk of neuro-developmental disorders (NDDs) in children born to men treated with valproate in the 3 months prior to conception compared to those born to men treated with lamotrigine or levetiracetam. • Other observational population-based studies did not show an increased risk of NDDs in children born to men treated with valproate as monotherapy in the 3-4 months prior to conception compared with men treated with lamotrigine or levetiracetam as monotherapy. • Differences in study design, including control for confounding and population selection, may contribute to differences in study findings. In addition, available data suggest that factors other than valproate exposure, including underlying paternal disease, may contribute to the observed association. Overall, the evidence regarding an increased risk of NDDs in children of fathers treated with valproate in the 3 months prior to conception is inconsistent, and the causal role of valproate is uncertain. • Discuss the need for male patients to consider a barrier method (condoms) and their female partner to consider effective contraception (birth control), as a precautionary measure while using valproate and for at least 3 months after treatment discontinuation. • Male patients should not donate sperm during treatment or for at least 3 months after treatment discontinuation.	

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Step 2: Specialist prescriber: Explain the risks to the patient or responsible person (continued)

Information to be discussed with the patient or responsible person	Initial to confirm you have discussed
Risks of stopping valproate without medical advice • Patients on valproate should not stop taking their medicine or change their dose unless they are told to do so by a specialist. • This is because their condition may become worse, including an increase in seizures in patients treated for epilepsy and an increased risk of relapse in patients treated for bipolar disorder.	

Step 3: To be completed by the patient or responsible person

Completing this section of the form confirms that you, the patient (or your responsible person), have discussed and acknowledge the risk of male infertility, the possible risk in children born to fathers treated with valproate, and the toxic effects of valproate on the testes of animals receiving valproate.
It is recommended that you keep a copy of this form which will also be added to your medical notes.

I have discussed the benefits and risks of valproate compared to other treatments with my specialist prescriber and I acknowledge that:	Initial to confirm you acknowledge each item
• Valproate may cause infertility in some male patients and that this infertility may be reversible after valproate is stopped or after the dose is reduced for some patients.	
• There are animal studies showing that valproate may have an effect on testes (testicles) and it is unclear what this means for humans.	
• Valproate may have a possible risk of neurodevelopmental conditions (problems with early childhood development) in children born to fathers treated with valproate in the 3 months before conception.	
• I am aware of the need to consider a barrier method (condoms) and the need for my female partner to consider an effective contraception (birth control) as a precautionary measure during treatment and for 3 months after stopping treatment to allow for one completed sperm cycle not exposed to valproate.	
• I need to consult my specialist when I am planning to conceive a child and before stopping contraception (birth control).	
• I should not donate sperm during treatment or for at least 3 months after treatment discontinuation.	
• I should not stop valproate or change the dose unless told to do so by my specialist as my condition may become worse, including an increase in seizures in patients treated for epilepsy and an increased risk of relapse in patients treated for bipolar disorder. • If my condition becomes worse, I should contact my specialist straight away.	
• I have been offered the Patient Guide and know where I can access this information online using the QR code on the leaflet in the pack.	
Name of patient:	
Name of responsible person (if applicable):	
Signature of patient (or responsible person):	**Date:**

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.

Please report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme, via the Yellow Card website https://yellowcard.mhra.gov.uk/, the free Yellow Card app available in Apple App Store or Google Play Store, and also some clinical IT systems for healthcare professionals. Alternatively, you can call 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

By reporting adverse drug reactions, you can help provide more information on the safety of this medicine.