

Valproate: reducing the reproductive risks

SAFETY

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Background

Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell) is a drug that is commonly used to treat epilepsy and bipolar disorder and occasionally migraine and headache conditions.

Exposure to valproate during pregnancy is associated with physical birth defects in 11% of babies and neurodevelopmental disorders in up to 30-40% of children, which may lead to permanent disability. An increased risk of neurodevelopmental disorders in children of fathers treated with valproate in the three months prior to conception is also possible however the causal role of valproate is not confirmed.

In November 2023, the MHRA issued a National Patient Safety Alert for organisations to prepare for new regulatory measures from January 2024 for the oversight of new and existing prescribing of valproate to female patients and other individuals assigned female at birth. Integrated Care Boards (ICBs) were instructed to co-ordinate the implementation of these measures and the actions set out in the alert. In September 2024 further advice was provided for male patients and other individuals assigned male at birth.

The regulatory change in January 2024, for valproate medicines, means that:

- Valproate must not be started in new patients 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.
- At their next annual specialist review, female patients and other individuals who were assigned female at birth 55 years and younger should be reviewed using a revised valproate Annual 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.
- At their next annual medication review, male patients and other individuals who were assigned male at birth of any age who may father a child should be informed about the possible risk of their child being diagnosed with a neurodevelopmental disorder.

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Safety and education materials

- [Annual Risk Acknowledgement Form for female patients](#) (ARAF): 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
- [Risk Acknowledgement Form for male patients](#) (RAF): 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 guide for women](#): provides those taking valproate (or their parent, caregiver, or responsible person) with updated information on the risks of valproate in pregnancy and what they need to do.
- [Patient guide for men](#): provides those taking valproate (or their parent, caregiver, or responsible person) with updated information on the risks to male patients and what they need to do.
- [Patient card](#): provides key information for patients receiving valproate on contraception and pregnancy prevention.
- [Booklet for healthcare professionals](#): 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.
- [Valproate use in women, girls of childbearing age and boys – guidance](#). Royal College of Paediatrics and Child Health (2024)
- [Contraception for Women Aged over 40 Years](#). Faculty of Sexual and Reproductive Health (FSRH) (August 2017, amended July 2023)
- [Advice for male patients on valproate to use contraception](#) and a [visual risk diagram](#). MHRA (2024)
- [Information leaflet about medicine reviews for women and people taking valproate](#). NHS South East Clinical Delivery and Networks (2024).

Contraception information and advice services

Cheshire East	Axess sexual health https://www.axess.clinic/
Cheshire West	www.thesexualhealthhub.co.uk
Halton	Axess sexual health https://www.axess.clinic/
Knowsley	Axess sexual health https://www.axess.clinic/
Liverpool	General Practice (all routine methods) and then LARC at specific PCN hubs. Axess sexual health https://www.axess.clinic/
Sefton	https://seftonsexualhealth.nhs.uk/
St Helens	https://www.sexualhealthsthelens.nhs.uk/
Warrington	Axess sexual health https://www.axess.clinic/
Wirral	www.sexualhealthwirral.nhs.uk

Clinical system coding

Reports on the valproate dashboard are informed by data extracted from clinical systems using these codes. The reliability of the dashboard reports relies on consistency of coding and these codes should be used preferentially.

	System One code	SNOMED Concept ID
Referral for completion of Valproate Annual Risk Acknowledgement Form: a referral has been made from primary care to the patient's specialist.	Y38a6	1366381000000107
Valproate Annual Risk Acknowledgement Form completed: an Annual Risk Acknowledgement Form (ARAF) has been received from the patient's specialist.	Y362e	1366401000000107
Pregnancy Prevention Programme started: an ARAF has been received from the patient's specialist with a decision to prescribe and the risk minimisation measures discussed with the patient.	Y2f16	1129771000000103
Pregnancy Prevention Programme not needed: an ARAF has been received from the patient's specialist with a decision to prescribe but there is no risk of pregnancy. For example, a female patient younger than 55 years that has had a hysterectomy.	Y2f18	1129791000000104
Did not attend Pregnancy Prevention Programme.	Y2f1a	1129831000000106
Pregnancy Prevention Programme declined: a patient referred to their specialist for an ARAF did not attend the appointment or declined to participate in the Pregnancy Prevention Programme.	Y2f17	1129801000000100
Pregnancy Prevention Programme discontinued.	Y2f19	1129841000000102
Pregnancy Prevention Programme declined by parent.	Y2f1b	1129821000000109
Pregnancy Prevention Programme declined by caregiver.	Y2f1c	1129811000000103
Risk Acknowledgement Form for Male Patients Starting Valproate completed	Ycj8h	2078961000000109
Valproate therapy stopped	Y39e8	1751131000000107

Effective contraception

Where there is a need to use effective contraception, the specialist must ensure that the patient is capable of complying with the need to use effective contraception and refer the patient for contraceptive advice if they are not using effective contraception.

At least one effective method of contraception, preferably a highly effective user independent form such as an intra-uterine device or implant or two complementary forms of contraception including a barrier method should be used.

Specialists should communicate the discussion about contraception to general practice using the [template letter](#) (see page 24) to supplement to the risk acknowledgment form and the clinic letter.

For further advice refer to the FSRH Clinical Effectiveness Unit (CEU) Statement: [Contraception for women using known teratogenic drugs or drugs with potential teratogenic effects](#) (February 2018) and the MHRA Drug Safety Update [Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed?](#) (March 2019).

Secondary care roles and responsibilities for new and existing patients

In all scenarios, consider the individual needs and circumstances of the patient, for example, language and mental capacity.

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
01. New initiation and reinitiation of valproate (all patients under the age of 55) For further guidance, please see Healthcare Professional Guide	<ul style="list-style-type: none"> Complete a risk acknowledgement form (ARAF or RAF) with the patient or responsible person: <ul style="list-style-type: none"> Obtain second signature on the form Pregnancy test where applicable Refer for contraceptive advice as needed Provide patient information booklet Book patient in for next review Store the completed form digitally in local system(s) Share completed form and letters digitally with general practice and patient Initiate prescribing and retain patient under their specialist prescriber care 	Non specialist prescribing after specialist secondary care initiation: <ul style="list-style-type: none"> Check indication for prescribing of valproate Check patient has completed risk acknowledgement form (ARAF or RAF) with double signature on local electronic patient record (EPR) or C&M shared care record (if and when available) Ensure satisfied that contraceptive advice has been provided, where applicable, if not discuss with patient Prescribe valproate 	<ul style="list-style-type: none"> Check patient has completed risk acknowledgement form (ARAF or RAF) with double signature on local electronic patient record or C&M shared care record (if and when available) Ensure valproate medicines are dispensed in manufacturer's original full pack*. All packs must have a "White Box" warning label on the packaging Ensure Patient Card is provided with every valproate pack dispensed (and, if present, the patient understands its content) <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk assessment is in place that refers to the need for different packaging.</p>
02. Existing female patients and other individuals who were assigned female at birth already taking valproate (patients under the age of 55)	<ul style="list-style-type: none"> Identify when last annual risk acknowledgement form (ARAF) completed and ensure a double signature has previously been obtained 	Non specialist prescribing after specialist secondary care initiation: <ul style="list-style-type: none"> Check indication for prescribing of valproate 	<ul style="list-style-type: none"> Check patient has completed ARAF within the last 12 months on local electronic patient record or C&M shared care record (if and when available)

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
<p>For further guidance, please see Healthcare Professional Guide</p>	<ul style="list-style-type: none"> • Complete ARAF with the patient or responsible person: <ul style="list-style-type: none"> – Obtain second signature if not previously obtained – Refer for contraceptive advice as needed – Provide patient information leaflet, if required • Book patient in for next review • Store the completed ARAF digitally in local system(s) • Share completed ARAF and letters digitally with general practice and patient 	<ul style="list-style-type: none"> • Ensure patient has had a completed ARAF within last 12 months on local electronic patient record or C&M shared care record (if and when available) • Ensure satisfied that contraceptive advice has been provided, where applicable, if not discuss with patient • Prescribe valproate 	<ul style="list-style-type: none"> • Ensure valproate medicines are dispensed in manufacturer's original full pack*. All packs must have a "White Box" warning label on the packaging • Ensure patient has received a Patient Card and understands the content. Provide a card if required. <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk assessment is in place that refers to the need for different packaging.</p>
<p>03. Existing male patients and other individuals who were assigned male at birth already taking valproate (patients of any age who may father a child)</p> <p>For further guidance, please see Healthcare Professional Guide</p>	<ul style="list-style-type: none"> • RAF is not required. • Inform patients of the possible risk • Recommend effective contraception until three months after the end of treatment • Ask whether planning a family in the next year and discuss alternative treatment options if they are • Advise to not donate sperm until three months after the end of treatment 	<ul style="list-style-type: none"> • Check indication for prescribing valproate • RAF is not required. • Inform patients of the possible risk • Recommend effective contraception until three months after the end of treatment • Ask whether planning a family in the next year and refer them to their specialist if they are • Advise to not donate sperm until three months after the end of treatment • Prescribe valproate 	<ul style="list-style-type: none"> • RAF is not required. • Ensure valproate medicines are dispensed in manufacturer's original full pack *. All packs must have a "White Box" warning label on the packaging • Ensure patient has access to a Patient Guide and understands the content. Provide a guide if required. <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk assessment is in place</p>

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
			that refers to the need for different packaging.
04. Patients in an acute care setting who are already taking valproate (all patients under the age of 55) Healthcare Professional Guide	<ul style="list-style-type: none"> Carry out steps as per existing female patients or existing male patients. 	<p>Female patients and other individuals assigned female at birth</p> <ul style="list-style-type: none"> Enquire about possibility of patient being pregnant and consider a urine or blood HCG test if there are concerns depending on the clinical need at the time Identify ARAF and document but this should not delay prescribing If there is no ARAF or a second specialist signatory is still required, consult with the relevant specialist to request ARAF completion <p>Male patients and other individuals assigned male at birth – no action is required, and prescribing should not be delayed. If the use of valproate is reviewed ensure the patient is aware of the reproductive risks.</p>	Not applicable
05. Patients in an acute care setting who are pregnant	<ul style="list-style-type: none"> Carry out steps as per patient is taking valproate and confirms they are pregnant 	<ul style="list-style-type: none"> Discuss with a senior clinician and specialist neurology or psychiatry services for consultant advice prior to prescribing 	

Primary care roles and responsibilities for new and existing patients

In all scenarios, consider the individual needs and circumstances of the patient, for example, language and mental capacity.

Scenario	General practice (non-specialist prescriber)	Pharmacist (Community)
06. New patients starting valproate (all patients under the age of 55)	<p>Each practice to agree internal process:</p> <ul style="list-style-type: none"> • Code on system that a risk acknowledgement form (ARAF or RAF) has been completed • Save completed form and letters on patients record • If patient using long-active reversible contraception (LARC), add date when due to be changed <p>Initial GP prescribing after specialist secondary care initiation:</p> <ul style="list-style-type: none"> • Check indication for prescribing of valproate • Check patient has completed form with double signature in GP clinical system or C&M Shared Care Record (if and when available) • Ensure satisfied that contraceptive advice has been provided, where applicable, if not discuss with patient • Prescribe valproate • Consider adding date the risk acknowledgement form was completed under prescribing directions (good practice) 	<ul style="list-style-type: none"> • Ensure valproate medicines are dispensed in manufacturer's original full pack*. All packs must have a "White Box" warning label either on the packaging • Ensure Patient Card is provided with every valproate pack dispensed (and, if present, the patient understands its content) <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk assessment is in place that refers to the need for different packaging.</p>
07. Existing female patients and other individuals who were assigned female at birth already taking valproate (patients under the age of 55)	<p>Each practice to agree internal process:</p> <ul style="list-style-type: none"> • Code on system that an ARAF has been completed • Save completed ARAF and letters on patients record • If patient using LARC, add date when due to be changed <p>Prior to repeat prescribing or annual medication review:</p> <ul style="list-style-type: none"> • Ensure patient has had a completed ARAF within last 12 months in GP clinical system or C&M Shared Care Record (if and when available) 	<ul style="list-style-type: none"> • Ensure valproate medicines are dispensed in manufacturer's original full pack*. All packs must have a "White Box" warning label either on the packaging • Ensure Patient Card is provided with every valproate pack dispensed (and, if present, the patient understands its content) <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient</p>

Scenario	General practice (non-specialist prescriber)	Pharmacist (Community)
	<ul style="list-style-type: none"> • Ensure satisfied that contraceptive advice has been provided, where applicable, if not discuss with patient • Prescribe valproate • Consider adding date ARAF completed under prescribing directions (good practice) 	<p>basis. This can only happen where a risk assessment is in place that refers to the need for different packaging.</p>
08. Existing male patients and other individuals who were assigned male at birth already taking valproate (patients of any age who may father a child)	<ul style="list-style-type: none"> • RAF is not required. • Inform patients of the possible risk at annual medication review. • Recommend effective contraception until three months after the end of treatment • Ask whether planning a family in the next year and if they are, refer them to their specialist for a discussion about the risks and treatment options • Advise to not donate sperm until three months after the end of treatment • Prescribe valproate 	<ul style="list-style-type: none"> • RAF is not required. • Ensure valproate medicines are dispensed in manufacturer's original full pack *. All packs must have a "White Box" warning label on the packaging • Ensure patient has access to a Patient Guide and understands the content. Provide a guide if required. <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk assessment is in place that refers to the need for different packaging.</p>

Secondary care specific scenarios

In all scenarios, consider the individual needs and circumstances of the patient, for example, language and mental capacity.

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
09. Female patients and other individuals who were assigned female at birth request a prescription for valproate but do not have an in-date ARAF in place or visible	<ul style="list-style-type: none"> • See patient within three weeks (face to face or virtual as required) • Arrange prescribing for the next supply of medication. • Carry out steps as per existing female patients 	<ul style="list-style-type: none"> • Document prescribing decision and actions in medical records/EPR • Refer the patient to specialist prescriber with request to be seen urgently within three weeks • Referral to be made within 48 hours 	<ul style="list-style-type: none"> • Continue to dispense if prescription presented • Ensure valproate medicines are dispensed in manufacturer's original full pack*. All packs must have a "White Box" warning label on the packaging • Ensure Patient Card is provided with every valproate pack dispensed (and, if present, the patient understands its content) • If making an emergency supply, consider supplying a manufacturer's full pack if it does not exceed the 30-day limit. <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk assessment is in place that refers to the need for different packaging.</p>

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
10. Female patients and other individuals who were assigned female at birth not under the care of a secondary care specialist or patient not been seen by specialist for more than 13 months	<ul style="list-style-type: none"> Accept referral and see patient within three weeks Arrange prescribing for the next supply of medication. Carry out steps as per existing female patient 	<ul style="list-style-type: none"> Document prescribing decision and actions in medical records/EPR Refer the patient to specialist prescriber with request to be seen urgently within three weeks Referral to be made within 48 hours 	<ul style="list-style-type: none"> Continue to dispense if prescription presented Ensure valproate medicines are dispensed in manufacturer's original full pack*. All packs must have a "White Box" warning label on the packaging Ensure Patient Card is provided with every valproate pack dispensed (and, if present, the patient understands its content) If making an emergency supply, consider supplying a manufacturer's full pack if it does not exceed the 30-day limit. <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk assessment is in place that refers to the need for different packaging.</p>
11. Patient confirms they are planning to start a family	<ul style="list-style-type: none"> See patient within three weeks 	<ul style="list-style-type: none"> Remind patient of risks and advise to continue with contraception until they seek specialist advice Provide patient information leaflet Signpost patient to inform their GP Refer the patient to secondary care specialist prescriber to be seen urgently within three weeks 	<ul style="list-style-type: none"> Remind patient of risks and to read their patient information leaflet or Patient Card Advise patient not to stop and continue taking valproate until specialist advice has been sought Signpost patient to inform their GP and contact their secondary care specialist prescriber to be seen urgently within three weeks

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
		<ul style="list-style-type: none"> Referral to be made within 48 hours 	
12. Patient is taking valproate and confirms they are pregnant	<ul style="list-style-type: none"> Epilepsy or Mental Health Specialist to make decision on which clinic is most appropriate and see patient as soon as possible and no later than three weeks 	<ul style="list-style-type: none"> Advise patient not to stop and continue taking valproate until specialist advice has been sought Inform GP and secondary care specialist prescriber that patient is pregnant As appropriate, refer to antenatal clinic or termination of pregnancy clinic with request to be seen in seven days (by a consultant with a special interest in high-risk pregnancies or maternal medicine or physician who works in a joint medical obstetrics clinic) Refer the patient to be seen urgently within three weeks Referrals to be made within 48 hours 	<ul style="list-style-type: none"> Remind patient of risks and to read their patient information leaflet or Patient Card Advise patient not to stop and continue taking valproate until specialist advice has been sought Signpost patient to inform their GP and contact their secondary care specialist prescriber as soon as possible.
13. Partner of a patient on valproate is pregnant, or they are planning a pregnancy, including those undergoing IVF	<ul style="list-style-type: none"> Refer urgently for pre-conception counselling 	<ul style="list-style-type: none"> Refer urgently for pre-conception counselling 	<ul style="list-style-type: none"> Signpost patient to inform their GP as soon as possible
14. Female patients and other individuals who were assigned female at birth Did Not Attend (DNA) their specialist appointment and their ARAF is out of date by three weeks or more	<p>For children and vulnerable patients – consider referral to safeguarding</p> <p>First DNA</p> <ul style="list-style-type: none"> Contact general practice – inform them about the DNA; ensure you have up to date contact details; 	<ul style="list-style-type: none"> Document prescribing decision and actions in medical records/EPR Refer the patient to specialist prescriber with request to be seen urgently within three weeks 	<ul style="list-style-type: none"> Remind patient of risks and to read their patient information leaflet or Patient Card Advise patient not to stop and continue taking valproate until specialist advice has been sought

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
	<p>share the clinical plan if the patient fails to engage</p> <ul style="list-style-type: none"> Offer the patient another appointment within three weeks – confirm by telephone; explain the plan should the patient fail to engage. <p>Second DNA</p> <ul style="list-style-type: none"> Contact general practice – inform them about the DNA; accept prescribing responsibility back 	<ul style="list-style-type: none"> Referral to be made within 24 hours 	
<p>15. Newly registered female patients and other individuals who were assigned female at birth request valproate, but their medical notes are not available, for example, patient new to area, or migrant</p>	<ul style="list-style-type: none"> Accept referral and see patient urgently within three weeks Arrange prescribing for the next supply of medication. Carry out steps as per existing female patient 	<ul style="list-style-type: none"> Ask patient if they have a copy of their latest ARAF Identify which (if any) secondary care service they had dealt with request a copy of the ARAF. Consider individual risk to patient of prescribing for four weeks (possibility of additional four weeks) to follow up ARAF completion vs not prescribing Document prescribing decision and actions in medical records/EPR If required, refer the patient to secondary care specialist prescriber with as much information as possible, and request to be seen urgently within three weeks Referral to be made within 48 hours 	<ul style="list-style-type: none"> Remind patient of risks and to read their patient information leaflet or Patient Card Advise patient not to stop and continue taking valproate until specialist advice has been sought

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
<p>16. Female patients and other individuals who were assigned female at birth who do not want to use effective contraception (continued use needed to meet the conditions of the pregnancy prevention programme)</p>	<ul style="list-style-type: none"> • Discuss the reasons for considering effective contraception with patient and/or parents • Document reason for not wishing to use effective contraception • Consider the risks and benefits of prescribing valproate • If the decision is to continue valproate, complete ARAF and provide patients with information booklet • Retain prescribing responsibility. 	<ul style="list-style-type: none"> • Discuss the reasons for considering effective contraception with patient and/or parents • Document reason for not wishing to use effective contraception • Consider individual risk to patient of prescribing for four weeks (if the patient has run out of medication) to enable referral back to specialist • Document prescribing decision and actions in medical records/EPR • Refer the patient to secondary care specialist with request to be seen urgently within three weeks • Referral to be made within 48 hours 	<ul style="list-style-type: none"> • Remind patient of risks and to read their patient information leaflet or Patient Card • Advise patient not to stop and continue taking valproate until specialist advice has been sought
<p>17. Female patients and other individuals who were assigned female at birth aged 10 to 15 years and post-menarche advise they are not sexually active and therefore do not wish to use effective contraception</p> <p>For further guidance, please see Valproate use in women, girls of childbearing years and boys</p>	<ul style="list-style-type: none"> • Discuss the reasons for considering effective contraception with patient, parents, or both • Document reason for not wishing to use effective contraception • Consider the risks and benefits of prescribing valproate • If the decision is to continue valproate, complete ARAF and provide patients with information booklet • Retain prescribing responsibility. 	<ul style="list-style-type: none"> • Discuss the reasons for considering effective contraception with patient and/or parents • Document reason for not wishing to use effective contraception • Consider individual risk to patient of prescribing for four weeks (if the patient has run out of medication) to enable referral back to specialist • Document prescribing decision and actions in medical records/EPR 	<ul style="list-style-type: none"> • Remind patient of risks and to read their patient information leaflet or Patient Card • Advise patient not to stop and continue taking valproate until specialist advice has been sought

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
		<ul style="list-style-type: none"> Refer the patient to secondary care specialist with request to be seen urgently within three weeks Referral to be made within 48 hours 	
18. Female patients and other individuals who were assigned female at birth transitioning from children to adult services	<ul style="list-style-type: none"> Planning and agreement of transfer to be undertaken with a valid ARAF in place for nine months post transition date <p>* Patient remains under the care of children's services until the patient has had their first appointment at adult services</p>	<ul style="list-style-type: none"> Check there is a transition letter from children's specialist service to adult services If transition letter received and there is an in-date ARAF in place (valid for at least nine months), prescribe valproate If no transition letter, document prescribing decision and actions in medical records/EPR <p>* Patient remains under the care of children's services until the patient has had their first appointment at adult services</p>	<ul style="list-style-type: none"> Remind patient of risks and to read their patient information leaflet or Patient Card Advise patient not to stop and continue taking valproate until specialist advice has been sought
19. Patient states they are post-menopausal For further guidance, please see Faculty of Sexual & Reproductive Healthcare (FSRH) Clinical Guideline contraception for women aged over 40 – diagnosing menopause	<ul style="list-style-type: none"> Age 40-50 years – consider stopping contraception after two years of spontaneous or natural amenorrhoea Age >50 years – may stop contraception after one year of spontaneous or natural amenorrhoea Continue to complete annual risk acknowledgement form (ARAF) until the age of 55 and share with the GP 	<ul style="list-style-type: none"> Age 40-50 years – consider stopping contraception after two years of spontaneous or natural amenorrhoea Age >50 years – may stop contraception after one year of spontaneous or natural amenorrhoea 	<ul style="list-style-type: none"> Remind patient of risks and to read their patient information leaflet or Patient Card

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
20. Patient requests supply of valproate during 'out of hours' period	Not applicable	Out of hours non-specialist prescribers: <ul style="list-style-type: none"> • Check indication for prescribing valproate • Check female patients and other individuals who were assigned female at birth have a completed ARAF with double signature on C&M shared care record (if and when available) • Ensure that contraceptive advice has been provided, where applicable, if not discuss with patient • If the ARAF is not in place or visible, consider the individual risk to the patient. Consider issuing a prescription for a supply sufficient to enable the patient to arrange further in-hours supply from their general practice. • Document prescribing decision and actions in medical records/EPR 	Not applicable
21. Health and Justice system considerations	<ul style="list-style-type: none"> • Carry out steps as per existing female patients or existing male patients. • Share completed ARAF with health and justice medical care team and patient 	<ul style="list-style-type: none"> • Check indication for prescribing valproate • Ensure female patients and other individuals assigned female at birth have a completed ARAF within last 12 months on C&M shared care record (if and when available) • Ensure satisfied that contraceptive advice has been 	Not applicable

Scenario	Secondary care (specialist prescriber)	Secondary care (non-specialist prescriber)	Pharmacist (Trust)
		<p>provided, where applicable, if not discuss with patient</p> <ul style="list-style-type: none"> • Document prescribing decision and actions in medical records/EPR 	

Primary care specific scenarios

In all scenarios, consider the individual needs and circumstances of the patient, for example, language and mental capacity.

Scenario	General practice (non-specialist prescriber)	Pharmacist (Community)
22. Female patients and other individuals who were assigned female at birth request a prescription for valproate but do not have an in-date ARAF in place or visible	<ul style="list-style-type: none"> • If there is no risk of pregnancy and the absence of risk is permanent, e.g., hysterectomy, continue to supply and raise an incident form about deviation from the agreed process. • If there is a risk of pregnancy or if the absence of risk may change, e.g., the patient is pre-menarche, issue one further one-month prescription and inform the patient that future prescribing will be from their specialist until a new ARAF is completed. • Document prescribing decision and actions in medical records/EPR • Refer the patient to secondary care specialist with a request to be seen urgently within three weeks • Referral to be made within 48 hours • Consider a mechanism to safety net or monitor that the referral was completed. 	<ul style="list-style-type: none"> • Continue to dispense if prescription presented • Ensure valproate medicines are dispensed in manufacturer's original full pack*. All packs must have a "White Box" warning label on the packaging • Ensure Patient Card is provided with every valproate pack dispensed (and, if present, the patient understands its content) • If making an emergency supply, consider supplying a manufacturer's full pack if it does not exceed the 30-day limit. <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk assessment is in place that refers to the need for different packaging.</p>
23. Female patients and other individuals who were assigned female at birth not under the care of a secondary care specialist or patient not been seen by specialist for more than 13 months	<ul style="list-style-type: none"> • If there is no risk of pregnancy and the absence of risk is permanent, e.g., hysterectomy, continue to supply and raise an incident form about deviation from the agreed process. • If there is a risk of pregnancy or if the absence of risk may change, e.g., the patient is pre-menarche, issue one further one-month prescription and inform the patient that future prescribing will be from their specialist until a new ARAF is completed. • Document prescribing decision and actions in medical records/EPR • Refer the patient to secondary care specialist with a request to be seen urgently within three weeks • Referral to be made within 48 hours 	<ul style="list-style-type: none"> • Continue to dispense if prescription presented • Ensure valproate medicines are dispensed in manufacturer's original full pack*. All packs must have a "White Box" warning label on the packaging • Ensure Patient Card is provided with every valproate pack dispensed (and, if present, the patient understands its content) • If making an emergency supply, consider supplying a manufacturer's full pack if it does not exceed the 30-day limit. <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk</p>

Scenario	General practice (non-specialist prescriber)	Pharmacist (Community)
	<ul style="list-style-type: none"> Consider a mechanism to safety net or monitor that the referral was completed. 	assessment is in place that refers to the need for different packaging.
24. Patient confirms they are planning to start a family	<ul style="list-style-type: none"> Remind patient of risks and advise to continue contraception until specialist advice has been sought Provide patient information leaflet Refer the patient to secondary care specialist prescriber to be seen within three weeks Referral to be made within 48 hours 	<ul style="list-style-type: none"> Remind patient of risks and to read their patient information leaflet or Patient Card Advise patient not to stop and continue taking valproate until specialist advice has been sought Signpost patient to inform their GP and contact their secondary care specialist prescriber to be seen urgently within three weeks
25. Patient is taking valproate and confirms they are pregnant	<ul style="list-style-type: none"> Advise patient not to stop and continue taking valproate until specialist advice has been sought Refer to secondary care specialist prescriber with advice that patient is pregnant Where appropriate, refer to antenatal clinic or termination of pregnancy clinic with request to be seen in seven days (by a consultant with a special interest in high-risk pregnancies or maternal medicine or physician who works in a joint medical obstetrics clinic) Refer the patient to be seen urgently within three weeks Referrals to be made within 48 hours 	<ul style="list-style-type: none"> Remind patient of risks and to read their patient information leaflet or Patient Card Advise patient not to stop and continue taking valproate until specialist advice has been sought Signpost patient to inform their GP and contact their secondary care specialist prescriber as soon as possible.
26. Partner of a patient on valproate is pregnant, or they are planning a pregnancy, including those undergoing IVF	<ul style="list-style-type: none"> Refer urgently for pre-conception counselling 	<ul style="list-style-type: none"> Signpost patient to inform their GP as soon as possible
27. Female patients and other individuals who were assigned female at birth DNA their specialist appointment and their ARAF is out of date by three weeks or more	First DNA <ul style="list-style-type: none"> Check patient details on the personal demographic service are correct Adding an expired ARAF message for the community pharmacy will also be seen in secondary 	<ul style="list-style-type: none"> Remind patient of risks and to read their patient information leaflet or Patient Card Advise patient not to stop and continue taking valproate until specialist advice has been sought

Scenario	General practice (non-specialist prescriber)	Pharmacist (Community)
	<p>care pharmacy as part of the national care record service (good practice).</p> <ul style="list-style-type: none"> • If a prescription is necessary, issue one further one-month prescription and inform the patient that future prescribing will be from their specialist until a new ARAF is completed. • Document prescribing decision and actions in medical records/EPR <p>Second DNA</p> <ul style="list-style-type: none"> • Repatriate the patient for the specialist to retain prescribing responsibility 	<ul style="list-style-type: none"> • As necessary, reiterate support for general practice about expired ARAF and prescribing returning to secondary care.
<p>28. Newly registered female patients and other individuals who were assigned female at birth request valproate, but their medical notes are not available, for example, patient new to area, or migrant</p>	<ul style="list-style-type: none"> • Ask patient if they have a copy of their latest ARAF • Identify which (if any) secondary care service they had dealt with request a copy of the ARAF. • If a prescription is required and the ARAF is not in place or visible, issue one further one-month prescription and inform the patient that future prescribing will be from their specialist until a new ARAF is completed. • Document prescribing decision and actions in medical records/EPR • Refer the patient to secondary care specialist with as much information as possible, and request to be seen urgently within three weeks • Referral to be made within 48 hours 	<ul style="list-style-type: none"> • Remind patient of risks and to read their patient information leaflet or Patient Card • Advise patient not to stop and continue taking valproate until specialist advice has been sought

Scenario	General practice (non-specialist prescriber)	Pharmacist (Community)
29. Female patients and other individuals who were assigned female at birth who have stopped or want to stop using effective contraception (continued use needed to meet the conditions of the pregnancy prevention programme)	<ul style="list-style-type: none"> • Discuss the reasons for considering effective contraception with patient and/or parents • Document reason for not wishing to use effective contraception • Issue one further one-month prescription and inform the patient that future prescribing will be from their specialist. • Document prescribing decision and actions in medical records/EPR • Refer the patient to secondary care specialist with request to be seen urgently within three weeks • Referral to be made within 48 hours 	<ul style="list-style-type: none"> • Remind patient of risks and to read their patient information leaflet or Patient Card • Advise patient not to stop and continue taking valproate until specialist advice has been sought
30. Female patients and other individuals who were assigned female at birth aged 10 to 15 years and post-menarche advise they are not sexually active and have stopped or want to stop using effective contraception For further guidance, please see Valproate use in women, girls of childbearing years and boys	<ul style="list-style-type: none"> • Discuss the reasons for considering effective contraception with patient and/or parents • Document reason for not wishing to use effective contraception • Issue one further one-month prescription and inform the patient that future prescribing will be from their specialist. • Document prescribing decision and actions in medical records/EPR • Refer the patient to secondary care specialist with request to be seen urgently within three weeks • Referral to be made within 48 hours 	<ul style="list-style-type: none"> • Remind patient of risks and to read their patient information leaflet or Patient Card • Advise patient not to stop and continue taking valproate until specialist advice has been sought
31. Female patients and other individuals who were assigned female at birth transitioning from children to adult services	<ul style="list-style-type: none"> • Check there is a transition letter from children's specialist service to adult services • If transition letter received and there is an in-date ARAF in place (valid for at least nine months), prescribe valproate • If no transition letter, document prescribing decision and actions in medical records 	<ul style="list-style-type: none"> • Remind patient of risks and to read their patient information leaflet or Patient Card • Advise patient not to stop and continue taking valproate

Scenario	General practice (non-specialist prescriber)	Pharmacist (Community)
	<p>* Patient remains under the care of children's services until the patient has had their first appointment at adult services</p>	
<p>32. Patient states they are post-menopausal</p> <p>For further guidance, please see Faculty of Sexual & Reproductive Healthcare (FSRH) Clinical Guideline contraception for women aged over 40 – diagnosing menopause</p>	<ul style="list-style-type: none"> • Age 40–50 years – Consider stopping contraception after two years of spontaneous or natural amenorrhoea • Age >50 years – May stop contraception after one year of spontaneous or natural amenorrhoea • An ARAF should continue to be completed until the age of 55 and shared with the GP. 	<ul style="list-style-type: none"> • Remind patient of risks and to read their patient information leaflet or Patient Card • Advise patient not to stop and continue taking valproate until specialist advice has been sought
<p>33. Patient requests supply of valproate during 'out of hours' period</p>	<p>Out of hours non-specialist prescribers:</p> <ul style="list-style-type: none"> • Check indication for prescribing valproate • Check female patients and other individuals who were assigned female at birth have a completed ARAF with double signature on GP clinical system or C&M Shared Care Record (if and when available) • Ensure that contraceptive advice has been provided, where applicable, if not discuss with patient. • If the ARAF is not in place or visible, consider the individual risk to the patient. Consider issuing a prescription for a supply sufficient to enable the patient to arrange further in-hours supply from their general practice. • Document prescribing decision and actions in medical records/EPR 	<p>For referrals for emergency supply via 111 or patient direct:</p> <ul style="list-style-type: none"> • If making an emergency supply, consider supplying a manufacturer's full pack if it does not exceed the 30-day limit. All packs must have a "White Box" warning label on the packaging • Ensure Patient Card is provided with every valproate pack dispensed (and, if present, the patient understands its content)
<p>34. Health and Justice system considerations</p>	<p>On receiving patients from health and justice facilities to primary care:</p>	<ul style="list-style-type: none"> • Continue to dispense if prescription presented • Ensure valproate medicines are dispensed in manufacturer's original full pack*. All packs must have a "White Box" warning label on the packaging

Scenario	General practice (non-specialist prescriber)	Pharmacist (Community)
	<ul style="list-style-type: none"> • Check indication for prescribing valproate • Ensure female patient or other individual assigned female at birth has had a completed ARAF within last 12 months on GP clinical system or C&M Shared Care Record (if and when available) • Ensure satisfied that contraceptive advice has been provided, where applicable, if not discuss with patient • If a prescription is required and the ARAF is not in place or visible, issue one further one-month prescription and inform the patient that future prescribing will be from their specialist until a new ARAF is completed. • Document prescribing decision and actions in medical records/EPR • Refer the patient to secondary care specialist with request to be seen urgently within three weeks • Referral to be made within 48 hours 	<ul style="list-style-type: none"> • Ensure Patient Card is provided with every valproate pack dispensed (and, if present, the patient understands its content) • If making an emergency supply, consider supplying a manufacturer's full pack if it does not exceed the 30-day limit. <p>* In rare cases, pharmacists can make an exception to the original full pack requirement on an individual patient basis. This can only happen where a risk assessment is in place that refers to the need for different packaging.</p>

Record of discussion on use of contraception for patients on valproate with childbearing potential

This document should be read in conjunction with the risk acknowledgment form and clinic letter.

Patient Name:
NHS Number:
Patient Date of Birth:
Indication for valproate:
Date of most recent risk acknowledgement form:
Date of risk acknowledgement form with double signature:

Contraception use (please select A or B)

☐ **A.** No contraception is being taken as the risk of pregnancy is low.

Reason:

OR

☐ **B.** The patient is using contraception as outlined below and has indicated an intent to continue to use this method over the next 12 months. (If a combination of e.g. barrier and hormonal contraception is proposed, please indicate both methods):

Highly effective contraceptive methods

Method	Tick if in use	Comment
Contraceptive implant		
Intrauterine system (IUS) hormone coil		
Intrauterine device – copper coil		
Female sterilisation		
Male sterilisation		

Other contraceptive methods

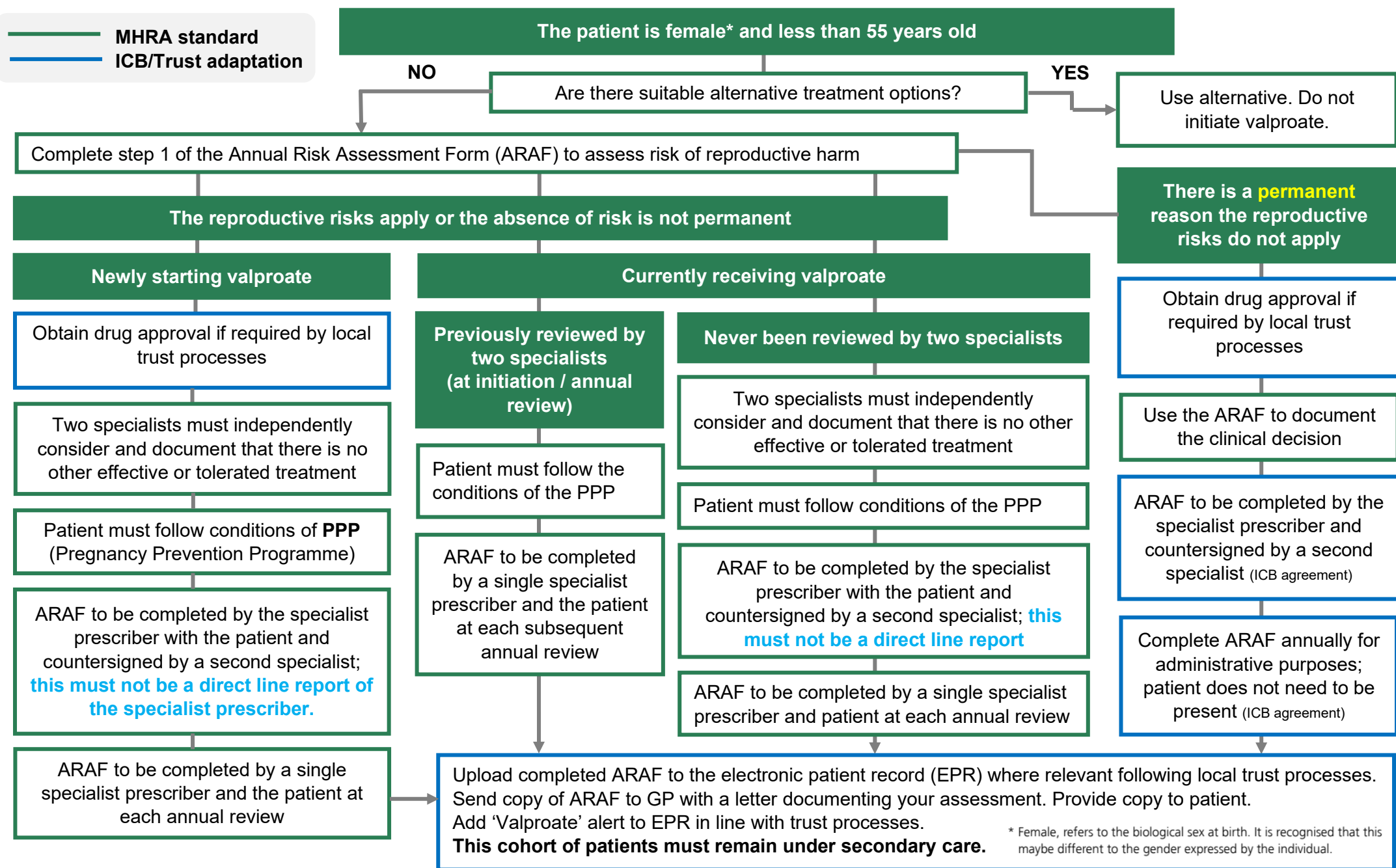
Method	Tick if in use	Comment
Combined oral contraceptive		
Progesterone only pill		
Combined transdermal patch		
Combined vaginal ring		
Progesterone only injectable		
Male condom		
Female condom		
Diaphragm with spermicide		
Other		

Having considered the risk and benefits and alternative treatments, I believe valproate is the most appropriate treatment for this patient and the patient has agreed to start or continue with valproate.

Specialist Name:
Role:
Specialist contact details:
Date record of discussion completed:

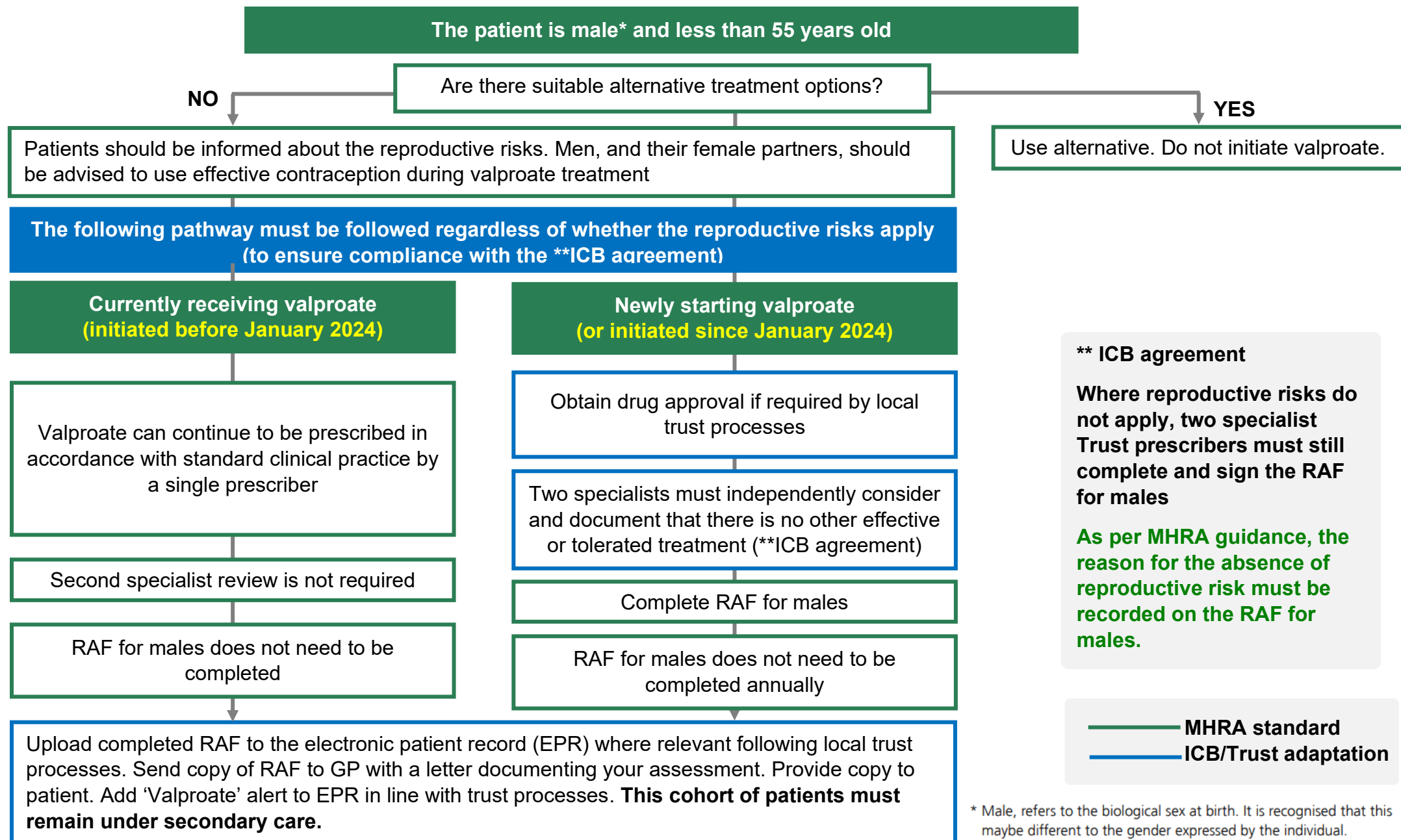
Specialist Trust risk minimisation measures for valproate prescribing

Valproate can seriously harm an unborn baby when taken during pregnancy and may lead to permanent disability in the offspring

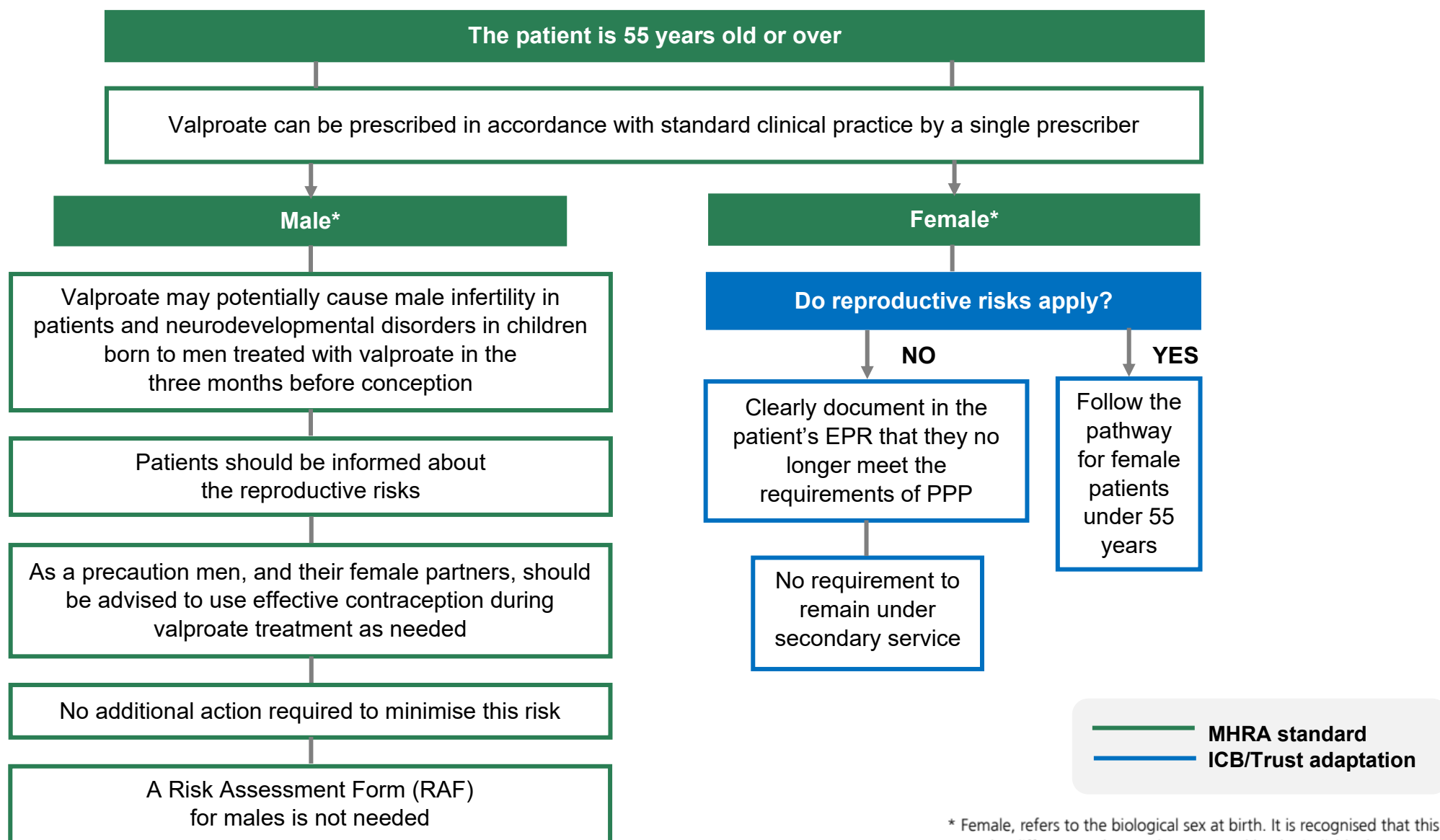


Specialist Trust risk minimisation measures for valproate prescribing

Valproate may potentially cause male infertility in patients and neurodevelopmental disorders in children born to men treated with valproate in the 3 months before conception



Specialist Trust risk minimisation measures for valproate prescribing



* Female, refers to the biological sex at birth. It is recognised that this maybe different to the gender expressed by the individual.

* Male, refers to the biological sex at birth. It is recognised that this maybe different to the gender expressed by the individual.

Primary Care risk minimisation measures for valproate prescribing

Children, young people and adults under 55 years of age

Follow local practice process to save the risk acknowledgement form and letter on patient's record using codes from the suggested list provided.

Female* patients

Initiated at any time
Continue prescribing if a double signature has previously been obtained, there is an in-date Annual Risk Assessment Form (ARAF), and effective contraceptive measures are assured.

Male* patients

Initiated before January 2024
Double signature not required.
Risk Assessment Form (RAF) not required.
Annual Risk Assessment Form (ARAF) not required.

Initiated since January 2024
Double signature **required**.
Risk Assessment Form (RAF) **required**.
Annual Risk Assessment Form (ARAF) not required.

Continue prescribing and recommend effective contraception

Patients are not discharged from specialist care

Urgently refer female patients for specialist review if a double signature has not previously been obtained, or if there is no in-date Annual Risk Assessment Form (ARAF), or if effective contraceptive measures are not assured.
Male patients under the care of The Walton Centre will be invited for review by the specialist team. All other male patients should ordinarily be routinely referred to the relevant trust.

Adults aged 55 years or more

Follow local practice process to record that the Pregnancy Prevention Programme no longer applies using codes from the suggested list provided.

Valproate can be prescribed in accordance with standard clinical practice

Good practice point: consider adding the date the risk acknowledgment form was completed under prescribing directions.

Good practice point: ensure processes are in place to identify and manage electronic medical records that have not automatically updated the National Care Record Service.

— MHRA standard
— ICB/Trust adaptation

* Female, refers to the biological sex at birth. It is recognised that this maybe different to the gender expressed by the individual.

* Male, refers to the biological sex at birth. It is recognised that this maybe different to the gender expressed by the individual.