

Humber and North Yorkshire ICS Shared Care Protocol: Valproate Medicines for Patients of Child-Bearing Potential

July 2024

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Approved: September 2024 – North Yorkshire and York APC and Humber APC & HNY IPMOC

Review: September 2026 or in line with national updates/review, whichever is soonest

The content of this shared care protocol was correct as of July 2024. As well as these protocols, please ensure that [summaries of product characteristics](#) (SPCs), [British national formulary](#) (BNF) or the [Medicines and Healthcare products Regulatory Agency](#) (MHRA) or [NICE](#) websites are reviewed for up-to-date information on any medicine.

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

The MHRA included requirements for care of men newly starting on valproate in their November 2023 update, however this is outside the scope of this Shared Care Protocol. For the purposes for this shared care patients of child-bearing potential is defined as patients able to conceive, carry and give birth to child.

Valproate should only be used in patients of child-bearing potential in line with the [Valproate Pregnancy Prevention Programme](#) and its use is contraindicated in pregnancy. Patients and/or carers must be given sufficient information regarding valproate efficacy and safety in order to allow shared decision making and balance the risks and benefits in deciding on the best treatment. Where a patient may be eligible, the shared care protocol is designed to support safe prescribing in strict accordance with current guidance. Valproate use in patients of child-bearing potential is continually under review from a safety perspective and national advice may be subject to change. Prescribers must ensure compliance with up-to-date guidance.

Additionally, the MHRA resources at:

<https://www.gov.uk/government/collections/valproate-safety-measures> provide information to support decision making along with relevant clinical information.

Specialist responsibilities

For new patients:

- Before prescribing valproate for a patient of child-bearing potential, including those who are likely to need treatment post-menarche, two specialists must independently consider and document that there is no other effective or tolerated treatment.

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (see above and [section 2](#)) and communicated to primary care.
- Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see [section 11](#)) to enable the patient to reach an informed decision. Counselling should include the need for highly effective contraception.
- Obtain and document patient consent. Provide appropriate information to patient/carer/responsible person and a copy of the [Prevent Patient Guide](#).
- If the patient lacks capacity, then the specialist is responsible for initiating a Best Interest Meeting/Process.
- Assess for contraindications and cautions (see [section 4](#)) and interactions (see [section 7](#)).
- Conduct required baseline investigations and initial monitoring (see [section 8](#)).
- Liaise with or refer to primary care or sexual health service to arrange for appropriate contraception.
- Initiate and optimise treatment as outlined in [section 5](#). Prescribe the maintenance treatment for at least 4 weeks and until optimised.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include a copy of the annual risk acknowledgement form (ARAF), and contact information for the specialist team ([section 13](#)).
- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the scheduled annual reviews and monitoring in [section 8](#) and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in [section 9](#) remains appropriate. Provide a copy of the updated ARAF to primary care each year (unless the assessment stopped at Step 1).

For existing patients:

- At their next annual specialist review from 2024 onwards, patients of childbearing potential and children who are pre- menarche should be reviewed using the revised valproate Risk Acknowledgement Form, which includes the need for a second specialist signature if the patient is to continue with valproate.
- Subsequent annual reviews are still required but with one specialist only unless the patient's situation changes.
- Fulfil their responsibilities under "**Prevent – the valproate pregnancy prevention programme**", (see [section 12](#)). This includes reassuming prescribing responsibilities and

providing advice on alternative treatment options if a patient becomes or wishes to become pregnant.

- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- If accepted, prescribe ongoing treatment as detailed in the specialist's request and as per [section 5](#), taking into any account any potential drug interactions in [section 7](#).
- Adjust the dose of valproate medicine prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in [section 9](#). Communicate any abnormal results to the specialist.
- Assess for possible interactions with valproate medicines when starting new medicines.
- Manage adverse effects as detailed in [section 10](#) and discuss with specialist team when required.
- Discuss urgently with the specialist about stopping valproate medicines if hepatotoxicity is suspected.
- Discuss urgently with the specialist if spontaneous bruising or bleeding occur.
- Fulfil their responsibilities under “**Prevent – the valproate pregnancy prevention programme**” (see [section 12](#)).
- Ensure the patient and/or carer has copies of the “**Prevent – the valproate pregnancy prevention programme**” materials, understands the need for highly effective contraception, and understands the advice in [section 11](#).
- Refer the management back to the specialist if the patient becomes or plans to become pregnant. Advise the patient not to stop taking valproate in the interim.
- Stop treatment only as advised by the specialist.
- Ensure the patient remains under the care of the specialist, is seen by them annually for a review, and always has an up-to-date ARAF on file.
- Continue to prescribe and dispense valproate but also discuss the current warnings and upcoming measures relating to valproate with patients and consider together how it affects the patient's individual circumstances.

Patient and/or carer responsibilities

- Take valproate medicines as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.

- Attend regularly for monitoring and review appointments with primary care prescriber and the specialist, and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend specialist appointments.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in [section 11](#).
- Be aware of the risks to an unborn baby when valproate is taken during pregnancy. Patients of child-bearing potential should use an appropriate form of contraception during treatment with valproate, as agreed with their doctor/nurse/sexual health service.
- Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant (see [section 11](#) and [section 12](#)).
- Report the use of any over the counter medications to their primary care prescriber and specialist, and be aware they should discuss the use of valproate medicines with their pharmacist before purchasing any OTC medicines.
- Moderate their alcohol intake to no more than 14 units per week (women). Avoid recreational drugs.
- Not to drive or operate heavy machinery if valproate affects their ability to do so safely. If unsure talk to their doctor, pharmacist, or healthcare professional (see [section 11](#)).

1. Background [Back to top](#)

This shared care protocol applies to prescribing in people who are biologically capable of becoming pregnant, from menarche to menopause. Shared care is not required for other patients at the moment. It is expected that both primary, secondary and tertiary care clinicians comply with its content following local agreement. All healthcare organisations are required to report valproate safety incidents and concerns, including those relating to valproate omission or avoidance, to their patient safety specialists through established reporting mechanisms.

Ethical considerations

People are still being born today exposed to sodium valproate in utero despite the fetotoxic and teratogenic risk being well recognised. Valproate has caused physical and neurodevelopmental harm and many of those exposed to valproate in utero have lifelong disabilities. However, it must also be acknowledged that valproate medicines are the most effective treatment for people with certain types of life-threatening epilepsy. To fulfil legal, GMC, and Montgomery judgement informed choice principles, patients and/or carers must be given appropriate information regarding valproate efficacy and safety in order to balance the risks and benefits and decide on the best treatment for them.

There are a number of innately complex practical and ethical considerations regarding valproate use and requirements of the “Prevent – the valproate pregnancy prevention programme”. In particular:

- People who are able to become pregnant and are unwilling to use long-term highly effective contraception for personal, religious, or health reasons.
- People who lack capacity. People with learning disabilities must not be presumed to not be sexually active.
- People with life-threatening symptoms that can only be controlled by valproate

For people who lack capacity to be involved in the decision-making process, the requirements of the Mental Capacity Act must be met. All patients should be reviewed by their specialist, who is responsible for assessing their capacity relating to decisions regarding choice of medication. Where appropriate the specialist should enter discussion with the GP regarding the patient’s capacity and decisions relating to contraception and childbearing. If the patient lacks capacity, then the specialist is responsible for initiating a Best Interest Meeting/Process.

Valproate medicines should not be used in patients of childbearing potential (including young girls who are likely to need treatment into their childbearing years) unless:

- other options are unsuitable, **and**
 - the pregnancy prevention programme (PPP) is in place, **or**
 - certain circumstances exist, such as those outlined below

The patient (or parent/caregiver/responsible person) must understand the risks and consent to treatment and agree to regular pregnancy testing as appropriate.

All patients should be reviewed by their specialist annually and valproate should be withdrawn where alternative and safer treatments are suitable. Any review should present the risks of withdrawing valproate or switching to alternative treatments, including the use of visual or other explanatory aids to support patients to understand their personalised risk. See section 11 [for information on risk communication materials and decision support tools](#). The risks of any loss of seizure control, a potential increased risk of sudden death in epilepsy (SUDEP), and deterioration of mental health on withdrawal of valproate should also be discussed. When deprescribing valproate, this should be tapered down gradually under the supervision of a specialist.

The conditions of “Prevent – the valproate pregnancy prevention programme” need to be maintained throughout the period of use of valproate medicines until discontinued. This includes patients who are switching to a therapy other than valproate medicines.

Exceptional circumstances when PPP is not appropriate/necessary:

- There are compelling reasons to indicate that there is no risk of pregnancy. The absence of risk may be permanent (e.g. patients who are post-menopausal or post-hysterectomy) or may change (e.g. patients who are pre-menarchal).
- The patient is unable or unwilling to use highly effective contraception for personal, religious or health reasons
- The patient lacks capacity to consent to sexual activity.

In these circumstances the decision to prescribe a valproate medicine must be made following careful discussion, with informed consent from the patient, parent, or carer, and, where appropriate, a Best Interests process. For circumstances in which a PPP is not appropriate, records must be kept of which decisions are taken, their justifications, and who was involved in decision-making. Clinicians are advised to observe advice from their healthcare regulators for such ethical considerations to ensure they meet statutory duties and professional responsibilities. The reasons why the patient does not need to be enrolled on the PPP should be documented on the ARAF. The patient or responsible person should countersign the ARAF where possible, to confirm the exception is in place and that risks have been discussed.

If the absence of risk may change, the date for the next annual review must be documented and the patient, parent or carer asked to contact the specialist rapidly if the situation changes before that date.

Full details of “**Prevent – the valproate pregnancy prevention programme**” and the accompanying risk management materials are available [from the MHRA website](#).

Available resources include:

- booklet for healthcare professionals
- booklet for patients
- patient card
- annual risk acknowledgement form (ARAF)

2. Indications

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- Epilepsy
- Treatment of mania in bipolar disorder
- Continuation of treatment after a manic episode

- Mood stabiliser in mood disorders and primary psychotic disorders, under the direction of a consultant psychiatrist ‡
- Prevention of atypical antipsychotic -induced seizures ‡
- Management of compulsive and aggressive behaviour ‡
- Migraine prophylaxis (**only** for existing patients as at June 2024)‡

‡ **Off-label indications. Please note licensed indications vary by form and manufacturer.**

Please see [SPCs](#) for details. Inclusion in the list above does not indicate that sodium valproate is appropriate to be prescribed in these off-label indications and NICE or other guidance on appropriateness should be reviewed prior to initiation. When prescribing valproate off-label, the specialist should be satisfied that an alternative, licensed medicine would not meet the patient's needs, in line with [GMC ethical guidance on prescribing unlicensed medicines](#).

3. Locally agreed off-label use [Back to top](#)

National scoping did not identify any additional appropriate off-label indications

4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see [BNF](#) & [SPC](#) for comprehensive information.

Contraindications:

- Hypersensitivity to valproate medicines or any other ingredient in the desired preparation
- Pregnancy (unless prescribed for epilepsy and no suitable alternative exists)
- In people of childbearing potential, unless the conditions of the pregnancy prevention programme are fulfilled
- Active liver disease
- Personal or family history of severe hepatic dysfunction, particularly drug-related
- Known or suspected mitochondrial disorders caused by mutations in the nuclear gene encoding the mitochondrial enzyme polymerase (POLG)
- Acute porphyrias
- Urea cycle disorders

Cautions:

- Hepatic impairment
- Systemic lupus erythematosus

- Renal impairment; dose reduction may be required
- Diabetes (ketone bodies may give false positive urinalysis results)
- Carnitine palmitoyltransferase (CPT) type II deficiency
- Alcohol consumption; manufacturers do not recommend during treatment with valproate. Patients should be advised to moderate their alcohol consumption to no more than 14 units per week for women.
- Suicidal ideation (see [MHRA advice](#) for more information).
- Weight or BMI above the healthy range.
- Long term use of valproate is associated with decreased bone mineral density. See [MHRA advice](#) for more information.

5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after at least 12 weeks, and when the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

Valproate medicines may only be initiated in people of child-bearing potential if the conditions of **Prevent** are fulfilled, or in other exceptional circumstances (see [section 1](#)).

Initial stabilisation:

The initial stabilisation period must be prescribed by the initiating specialist.

Sodium valproate or valproic acid:

Adults and children 12 years and over: 600 mg daily, increasing in 150-300 mg increments at intervals of at least 3 days until control is achieved. Slower titration may be appropriate, particularly in neurology.

Children over 20 kg: up to 400 mg daily, increased at intervals until control is achieved

Valproate semisodium:

Adults: up to 750 mg daily in 2-3 divided doses. Increased incrementally to the lowest dose which produces the desired effect.

Efficacy in children below 18 years has not been established.

Maintenance dose (following initial stabilisation):

The initial maintenance dose must be prescribed by the initiating specialist.

Sodium valproate or valproic acid:

Adults: Usually 1000 – 2000 mg daily, i.e., 20-30 mg/kg. Where adequate control is not achieved within this range the dose may be up to 2500 mg per day.

Children over 20 kg: Usually in the range 20-30 mg/kg daily. Maximum dose 35 mg/kg daily.

Valproate semisodium:

Adults: Usually 1000 – 2000 mg daily. Patients receiving daily doses exceeding 45 mg/kg daily should be carefully monitored.

Conditions requiring dose adjustment:

Dose reduction may be necessary in severe renal impairment; dose according to response.

6. Pharmaceutical aspects

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Route of administration:	Oral
Formulation:	<p>Sodium valproate</p> <ul style="list-style-type: none">• Epilim®▼<ul style="list-style-type: none">○ crushable tablets: 100 mg○ gastro-resistant tablets: 200 mg, 500 mg○ oral liquid or oral syrup: 200 mg/5 mL• Episenta®▼<ul style="list-style-type: none">○ modified-release capsules: 150 mg, 300 mg○ modified-release granules: 500 mg, 1000 mg• Epival CR®▼ modified-release tablets: 300 mg, 500 mg• Orlept®▼ gastro-resistant tablets: 200mg• Sodium valproate<ul style="list-style-type: none">○ Gastro-resistant tablets: 200 mg, 500 mg○ Oral solution: 40 mg/mL <p>Valproic acid</p> <ul style="list-style-type: none">• Convulex®▼ enteric coated capsules: 150 mg, 300 mg, 500 mg

	<p>Valproate semisodium</p> <ul style="list-style-type: none"> • Belvo®▼ gastro-resistant tablets: 250 mg, 500 mg • Depakote®▼ gastro-resistant tablets: 250 mg, 500 mg • Syonell®▼ gastro-resistant tablets: 250 mg, 500 mg <p>Sodium valproate / valproic acid</p> <ul style="list-style-type: none"> • Dyzantil®▼ modified-release tablets: 200 mg, 300 mg, 500 mg • Epilim®▼ Chrono controlled release tablets: 200 mg, 300 mg, 500 mg • Epilim®▼ Chronosphere modified release granules: 50 mg, 100 mg, 250 mg, 500 mg, 750 mg, 1000 mg
Administration details:	<p>Valproate medicines should preferably be prescribed as monotherapy and at the lowest effective dose.</p> <p>Doses should be taken regularly, at the same time every day.</p> <p>If a dose is missed, it should be taken as soon as remembered unless it is nearly time for the next dose. <u>A double dose should not be taken to make up for a missed dose.</u></p>
Other important information:	<p>Continuity of supply of a specific product</p> <p>The MHRA classify valproate medicines as a category 2 antiepileptic drug. When used for epilepsy, the need for continued supply of a particular manufacturer’s product should be based on clinical judgement and consultation with the patient and/or carer, considering factors such as seizure frequency and treatment history. See MHRA advice for more information. In case of availability problems, discuss with the specialist team for advice on the best course of action for the individual patient.</p> <p>False positive laboratory tests</p> <p>Valproate medicines may cause false positive urine tests for ketones.</p>

7. Significant medicine interactions

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Please see [BNF](#) or [SPC](#) for comprehensive information and recommended management.

8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

Baseline investigations (all indications):

If it is not possible to perform baseline investigations prior to initiation (e.g. in an emergency situation), they should be completed as soon as possible after initiation.

- Two specialists must independently consider and document in the ARAF that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.
- Share the completed ARAF with the patient's GP. Serum pregnancy test
- Urea and electrolytes & GFR
- Full blood count
- Liver function tests, including coagulation screen
- Height, weight, and BMI

Ongoing monitoring and advice:

As per new regulatory measures for valproate from January 2024, all patients that need to continue on valproate must have their treatment reviewed by two specialists and a new ARAF signed by both to confirm no other alternative treatment is suitable.

All patients should be reviewed by their specialist annually and valproate should be withdrawn where there are alternative and safer treatments available. Deprescribing should be undertaken under the supervision of a specialist.

Annual review should include:

- completion of the [Annual Risk Acknowledgement Form](#) and sharing of the form with the GP practice each year
- discussion regarding contraception, including a prompt to check when long-acting reversible contraceptives (e.g. implants, intrauterine devices) must be renewed

When a patient is reviewed, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in [section 9](#) remains appropriate.

9. Ongoing monitoring requirements to be undertaken by primary care

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See [section 10](#) for further guidance on management of adverse effects/responding to monitoring results.

Monitoring and advice	Frequency
<ul style="list-style-type: none"> • Full blood count • Liver function tests • Weight and BMI • Clotting screen (only required before surgery or following spontaneous bleeding/bruising) 	Six months after initiation, and annually thereafter
<p>Annual Risk Acknowledgement Form</p> <p>Ensure that the patient has had an annual review with their specialist, and:</p> <ul style="list-style-type: none"> • an up to date annual risk acknowledgment form is on file, or • there is a documented permanent absence of risk of pregnancy, e.g. the patient is post-menopause or has had a hysterectomy, or permanently lacks capacity to consent to sexual activity (see section 1) 	Annually
<p>Contraception</p> <p>Ensure that the patient has access to an appropriate method of contraception, knows how to use it, and is aware of the importance of using it correctly. Where appropriate, offer signposting to providers, e.g. community contraceptive clinic, or sexual health clinics</p>	At all patient contacts regarding valproate.

<p>and prompts to check when long-acting reversible contraceptives (e.g. implants, intrauterine devices) must be renewed.</p>	
<p>Pregnancy testing</p> <p>Discuss pregnancy testing and prompt patients to take a test when appropriate. Where possible, offer signposting to providers of free testing, e.g. community contraceptive clinic, or sexual health clinics.</p>	<p>At all patient contacts regarding valproate. Pregnancy testing is recommended:</p> <ul style="list-style-type: none"> • 3 weeks after starting a new contraceptive method, if there was any risk of pregnancy at the start of the contraceptive method • Whenever there is reason to suggest lack of adherence or effectiveness of contraception • More frequently in patients using a user-dependent method of contraception, e.g. condom, cap, diaphragm, oral contraceptive pills, or fertility awareness-based methods
<p>(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.</p>	
<p>10. Adverse effects and other management Back to top</p> <p>Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard</p> <p><u>For information on incidence of ADRs see relevant summaries of product characteristics</u></p>	
<p style="text-align: center;">Result</p>	<p style="text-align: center;">Action for primary care</p>
<p style="text-align: center;">As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance</p>	
<p>Pregnancy confirmed</p>	<p>Prescribe folic acid 5mg daily immediately, and refer to specialist and maternity/obstetrics service urgently (within days). Remind the patient not to stop taking valproate medicine in the interim.</p>

<p>Patient planning a pregnancy</p>	<p>Refer to specialist. Remind the patient not to stop using contraception or taking valproate medicine in the interim.</p>
<p>Full blood count: Red cell count, haemoglobin or platelets below reference range</p>	<p>Contact specialist team for advice; consider monitoring more frequently. Do not stop valproate medicine.</p>
<p>Spontaneous bruising or bleeding, or other signs or symptoms of blood dyscrasias, e.g. purpura, sore throat, fever, or malaise</p>	<p>Continue valproate medicine and discuss with specialist team urgently (same day). Full blood count, liver function tests, and coagulation screen are indicated; discuss most appropriate route with specialist team.</p>
<p>Liver function tests: Raised liver enzymes in isolation</p>	<p>Assess clinically and review for other causes. Monitor until return to normal. Do not stop valproate medicine. Hepatic enzymes alone are not always a good measure; assess in the context of coagulation screen, albumin, and bilirubin.</p>
<p>Signs and symptoms of liver dysfunction, e.g.:</p> <ul style="list-style-type: none"> - prolonged prothrombin time (particularly in association with significant decrease in fibrinogen and coagulation factors, decreased albumin, increased bilirubin and raised transaminases) - symptoms including asthenia, malaise, anorexia, lethargy, oedema, drowsiness, repeated vomiting and abdominal pain, jaundice - recurrence of seizures 	<p>Repeat LFTs and coagulation screen and discuss urgently with specialist team. Stopping valproate medicine may be indicated while waiting for results, particularly if there is strong suspicion that worsening seizures are due to hepatic dysfunction.</p>

<p>Gastrointestinal disorders:</p> <p>Symptoms of pancreatitis, e.g. acute abdominal pain, nausea, or vomiting</p>	<p>Refer for urgent hospital admission if the person has suspected acute pancreatitis, for further management.</p> <p>Do not delay admission by taking blood samples or ordering imaging in primary care.</p>
<p>Psychiatric disorders</p> <p>Suicidal ideation or behaviour</p>	<p>Refer for urgent psychiatric assessment via local pathways e.g. crisis or specialist teams, if appropriate. Notify specialist team. Do not stop valproate medicine.</p>
<p>Weight or BMI above the healthy range</p>	<p>Do not stop valproate medicine. Provide appropriate support on multicomponent interventions to increase physical activity levels, improve eating behaviour and quality of diet.</p> <p>Consider referral to dietitian or other local services if relevant comorbidities are present (e.g. heart disease, diabetes) or BMI >35.</p>

11. Advice to patients and carers

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The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient must report any of the following signs or symptoms to their primary care prescriber without delay:

- If she suspects there has been a problem with her contraception or she may be pregnant
- If she is planning a pregnancy
- Symptoms of blood disorders, e.g. unexplained bleeding, bruising, purpura, sore throat, fever, or malaise
- Symptoms of liver disorders, e.g. sudden weakness, malaise, anorexia, lethargy, oedema, drowsiness (especially if accompanied by repeating vomiting and abdominal pain), or jaundice.
- Symptoms of pancreatitis, e.g. abdominal pain, nausea, or vomiting

- Suicidal ideation or behaviour.

The patient should be advised to:

- **Not** stop taking valproate medicines without first discussing this with their doctor, especially if taking for epilepsy (risk of status epilepticus and sudden unexpected death in epilepsy (SUDEP)).
- **Ensure** other healthcare providers are aware of valproate medicine use (for example, coagulation blood tests may be needed prior to surgery).
- **Use an appropriate form of contraception**, as agreed with their doctor/nurse/sexual health service
- **Take a pregnancy test whenever they suspect there is a chance they could be pregnant.** This includes:
 - Three weeks after starting a new method of contraception, particularly if there was any risk of pregnancy at the start of the new method
 - Whenever there is any reason to doubt that contraception has been effective, e.g. missed pill, broken condom, missed or late menstrual period
 - Whenever a health professional recommends or offers a pregnancy test
- See NHS advice on when to do a pregnancy test, and where to get one:
<https://www.nhs.uk/pregnancy/trying-for-a-baby/doing-a-pregnancy-test/>
- Not drive or operate machines if valproate affects their ability to do so safely. Patients with a diagnosis which affects their ability to drive must notify the Driver and Vehicle Licensing Agency (DVLA); see <https://www.gov.uk/driving-medical-conditions>.
- Tell anyone who prescribes them a medicine that they are taking a valproate medicine. Always tell a pharmacist before purchasing any medicines over the counter, including herbal remedies, and ask if they are safe.
- Report any side effects to their primary care prescriber, e.g. weight gain.
- Valproate can affect bone density. People taking valproate should consider taking vitamin D supplements; see <https://www.nhs.uk/conditions/vitamins-and-minerals/vitamin-d/>.

Patient information:

NHS.uk, sodium valproate <https://www.nhs.uk/medicines/sodium-valproate/>

NHS.uk Contraception Guide: <https://www.nhs.uk/conditions/contraception/>

Pregnancy prevention programme patient guide and patient card: [Valproate use by women and girls - GOV.UK \(www.gov.uk\)](#)

MHRA: epilepsy medicines and pregnancy

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950069/Epilepsy-medicines-in-pregnancy-leaflet.pdf

12. Pregnancy, paternal exposure and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

Pregnancy:

Valproate medicines are associated with a significant risk of birth defects and developmental disorders in children born to patients who take valproate medicines during pregnancy. In patients of childbearing potential valproate medicines **must** be initiated and supervised by an appropriate specialist experienced in the management of the patient's condition. Valproate medicines **should not** be used in patients of childbearing potential unless other treatments are ineffective or not tolerated, or in circumstances as outlined in [section 1](#).

If valproate is prescribed, at least one highly effective method of contraception (preferably a user independent form such as an intrauterine device or implant) or two complementary forms of contraception including a barrier method should be used.

For children or patients without the capacity to make an informed decision, provide the information and advice on highly effective methods of contraception and on the use of valproate medicines during pregnancy to their parent(s)/caregiver(s)/ responsible person(s) and make sure they clearly understand the content.

Further information for healthcare professionals:

Further information on effective contraception: [Guidance Document on Valproate Use in Women and Girls of Childbearing Years - On behalf of the Royal College of General Practitioners and Association of British Neurologists and Royal College of Physicians](#)

Further information for patients: <https://www.medicinesinpregnancy.org/Medicine--pregnancy/Sodium-valproate/>

Breastfeeding:

Valproate medicines are suitable for use in breastfeeding but the conditions of "Prevent – the valproate pregnancy prevention programme" must be met, including that other treatments are ineffective or not tolerated, or in circumstances as outlined in [section 1](#)

Valproate is excreted in breast milk in small amounts. Infants should be monitored for adverse effects such as jaundice, bruising, and bleeding.

For more information see the following Specialist Pharmacy Service resources (login required – free to register):

- Safety in Lactation: Drugs for bipolar disorder <https://www.sps.nhs.uk/articles/treating-bipolar-disorder-during-breastfeeding/>

13. Specialist contact information

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Name: *[insert name]*

Role and specialty: *[insert role and specialty]*

Daytime telephone number: *[insert daytime telephone number]*

Email address: *[insert email address]*

Alternative contact: *[insert contact information, e.g. for clinic or specialist nurse]*

Out of hours contact details: *[insert contact information, e.g. for duty doctor]*

Valproate Safety Lead (Named Person)

Name: *[insert name]*

Role and specialty: *[insert role and specialty]*

Daytime telephone number: *[insert daytime telephone number]*

Email address: *[insert email address]*

14. Additional information

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Patients of childbearing potential on valproate **should not be removed from any active caseloads** of their doctor or specialist clinician.

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

The NHS Discharge Medicines Service is used to ensure better communication of any changes associated with the Prevent programme/annual risk acknowledgement form when they leave hospital and to ensure valproate safety measures are in place and appropriately communicated.

By referring patients to community pharmacy on discharge with information about medication changes made in hospital, community pharmacy can support patients to improve outcomes, prevent harm and exposure during pregnancy.

15. References

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16. Other relevant national guidance

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- NHSE Shared Care Guidance: <https://www.england.nhs.uk/medicines-2/regional-medicines-optimisation-committees-advice/shared-care-protocols/>
- NHSE – Responsibility for prescribing between primary & secondary/tertiary care. Available from <https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/>
- General Medical Council. Good practice in prescribing and managing medicines and devices: Shared care. Available from <https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care>
- NICE NG197: Shared decision making. Last updated June 2021. <https://www.nice.org.uk/guidance/ng197/>

17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

To be agreed and completed locally

18. Organisational responsibilities

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

Please see '**Prevent**' for comprehensive information. Additional recommendations beyond the 'Prevent' programme to facilitate the implementation of valproate safety across primary,

secondary and tertiary care have been listed here. All parties and involved should follow the recommendations of “**Prevent – the valproate pregnancy prevention programme**”.

Dispensing contractors' responsibilities

- Follow the recommendations of Prevent – the valproate pregnancy prevention programme, including providing a Patient Card every time valproate is dispensed and reminding patients of the risks in pregnancy, the need for highly effective contraception, and the need for annual specialist review. Ensure they have the ‘**Prevent**’ patient guide.

Providers of adult social care

- Support patients of childbearing potential to attend their primary care and /or specialist appointments for review.
- Provide information about “**Prevent – the valproate pregnancy prevention programme**”, this should be in an accessible format e.g., easy read, or relevant language if applicable.
- Hold a copy of the Annual Risk Acknowledgement Form if the patient is unable to do so themselves.
- Support patients of childbearing potential without the capacity to make an informed decision. Ensure they or their parent(s)/caregiver(s)/ responsible person(s) have been provided with information and advice on highly effective methods of contraception and on the use of valproate medicines during pregnancy, and make sure they clearly understand the content.
- If a pregnancy occurs, providers must support patients to seek advice from their specialist and obstetrician as soon as possible.

Sexual health services

- Enquire whether patients of child-bearing potential are taking any prescribed or over-the-counter medicines, including valproate, when providing contraceptive advice. Ensure adherence with highly effective contraception and communicate any challenges on providing or maintaining highly effective contraception to the patient’s primary or secondary care prescriber.

Organisations with specialists that prescribe valproate

- Where possible, provide a **Named Person** tasked with oversight of valproate safety measures to ensure they are in place and are adhered to such as:
 - a database of patients of childbearing potential on valproate and completion of the required annual risk acknowledgement form by the relevant specialist
 - a designated point of contact for primary care queries regarding non-adherence to the pregnancy prevention programme (PPP) or incomplete/expired annual risk acknowledgement forms

- ensuring relevant pathways, policies, procedures are in place to ensure valproate safety

Patient Safety Specialists and Trust Medication Safety Officers

- Be informed of measures to ensure valproate safety within the organisation and across primary, secondary and tertiary services.

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*

Date of birth: *[insert date of birth]*

NHS Number: *[insert NHS Number]*

Diagnosis: *[insert diagnosis]*

As per the agreed *[insert APC name]* shared care protocol for *[insert medicine name]* for the treatment of *[insert indication]*, this patient is now suitable for prescribing to move to primary care. The patient fulfils criteria for shared care and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
<i>The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:</i>	
<i>Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory</i>	Yes / No
<i>The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care</i>	Yes / No
<i>The risks and benefits of treatment have been explained to the patient</i>	Yes / No
<i>The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed</i>	Yes / No
<i>The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments</i>	Yes / No
<i>I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)</i>	Yes / No
<i>I have included with the letter copies of the information the patient has received</i>	Yes / No
<i>I have provided the patient with sufficient medication to last until</i>	
<i>I have arranged a follow up with this patient in the following timescale</i>	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*. If you are in agreement, please undertake monitoring and treatment from *[insert date]* NB: date must be at least 1 month from initiation of treatment.

The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

Please respond to this request for shared care, in writing, within 14 days of the request being made where possible.

Specialist Prescriber signature: _____ **Date:** _____

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*
Patient *[insert Patient's name]*
NHS Number *[insert NHS Number]*
Identifier *[insert patient's date of birth and/or address]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: _____ **Date:** _____

Primary Care Prescriber address/practice stamp

Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

Re:

Patient *[insert Patient's name]*
 NHS Number *[insert NHS Number]*
 Identifier *[insert patient's date of birth and/or address]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety NHS *[Humber & North Yorkshire ICB]*, in conjunction with local acute trusts have classified *[insert medicine name]* as a Shared Care drug and requires a number of conditions to be met before transfer can be made to primary care.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

		Tick which apply
1.	<p>The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care.</p> <p>As the patient's primary care prescriber I do not feel clinically confident to manage this patient's condition because <i>[insert reason]</i>. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice.</p> <p>I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.</p>	
2.	<p>The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement.</p> <p>As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time.</p> <p>Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you</p>	

3.	<p>A minimum duration of supply by the initiating clinician</p> <p>As the patient has not had the minimum supply of medication to be provided by the initiating specialist I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended.</p> <p><i>Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.</i></p>	
4.	<p>Initiation and optimisation by the initiating specialist</p> <p>As the patient has not been optimised on this medication, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended.</p> <p><i>Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.</i></p>	
5.	<p>Shared Care Protocol not received</p> <p>As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed.</p> <p>For this reason, I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible in order to provide them with the medication that you have recommended.</p> <p><i>Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.</i></p>	
6.	<p>Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)</p>	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and

the dissemination of sufficient, up-to-date information to individual GPs.” In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible.

Yours sincerely

Primary Care Prescriber signature: _____
Date: _____

Primary Care Prescriber address/practice stamp