NHS South West Yorkshire Partnership NHS Foundation Trust

NHS Barnsley Hospital NHS Foundation Trust

NHS Barnsley Clinical Commissioning Group

Shared Care Guideline for the use of anticonvulsants as mood stabilisers

Introduction

Indication/Licensing information

Semisodium valproate and sodium valprorate are used for the treatment of manic episodes associated with bipolar disorder.

Valproate (valproic acid and sodium valproate) is also used for the prophylaxis of bipolar disorder; however, it should **not** normally be prescribed for women of child-bearing potential.

All women and girls of childbearing potential being treated with valproate medicines must be supported on a Pregnancy Prevention Programme. These conditions are also applicable to female patients who are not sexually active unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy.

The Pregnancy Prevention Programme is a system of ensuring all female patients taking valproate medicines:
•have been told and understand the risks of use in pregnancy and have signed a Risk Acknowledgement Form
•are on highly effective contraception if necessary
•see their specialist at least every year

Details of the Pregnancy Prevention Programme can be found at https://www.gov.uk/drug-safety-update/valproate-medicines-epilim-depakote-pregnancy-prevention-programme-materials-online

Details of the pathway in SWYPFT can be found at Valproate reviews | South West Yorkshire Partnership NHS Foundation Trust

Further information on PPP during COVID pandemic can be found at Valproate Pregnancy Prevention Programme: temporary advice for management during coronavirus (COVID-19) - GOV.UK (www.gov.uk)

If treatment with valproate is stopped, reduce the dose gradually over at least 4 weeks

Dosage and administration
Mania, initially 750 mg daily in 2–3 divided doses, increased according to response, usual dose 1–2 g daily; doses greater than 45 mg/kg daily require careful monitoring

Carbamazepine may be used under specialist supervision for the prophylaxis of bipolar disorder (manic-depressive disorder) in patients unresponsive to a combination of other prophylactic drugs; it is used in patients with rapid-cycling manic-depressive illness (4 or more affective episodes per year). The dose of carbamazepine should not normally be increased if an acute episode of mania occurs.
When stopping treatment with carbamazepine, reduce the dose gradually over a period of at least 4 weeks.

Dosage and administration
Prophylaxis of bipolar disorder unresponsive to lithium by mouth, initially 400 mg daily in divided doses increased until symptoms controlled; usual range 400–600 mg daily; max. 1.6 g daily

Lamotrigine is licensed for the prevention of depressive episodes in patients with bipolar I disorder who experience predominantly depressive episodes in people over 18 years of age

Dosage and administration
Initially 25 mg once daily for 14 days, then 50 mg daily in 1–2 divided doses for further 14 days, then 100 mg daily in 1–2 divided doses for further 7 days; maintenance 200 mg daily in 1–2 divided doses, patients stabilised on lamotrigine for bipolar disorder may require dose adjustments if other drugs are added to or withdrawn from their treatment regimens—consult product literature, dose titration should be repeated if restarting after interval

of more than 5 days; maximum 400 mg per day.
Dosage is complex depending on co-prescribed medication – please see SPC for further details
http://www.medicines.org.uk/emc/medicine/4228

Responsibilities of the specialist initiating treatment

Summary

1, Initiate and stabilise treatment with semisodium or sodium valproate, carbamazepine or lamotrigine. To initiate therapy, arrange prescription and evaluate over the first 3 months

2. Discuss the benefits and side effects of treatment with the patient.

3. Valproate should not be prescribed to female children, female adolescents, women of childbearing potential or pregnant women unless other treatments are ineffective or not tolerated. Valproate is contraindicated in women and girls of childbearing potential unless there is a Pregnancy Prevention Programme in place. These conditions are also applicable to female patients who are not sexually active unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy. In pregnancy, valproate must only be used for epilepsy if there is no suitable alternative treatment.

Pregnancy prevention programme (Prevent)

If valproate is being used in woman of child bearing potential, ensure: the woman (or their carer) is made aware and understand the risks; is supplied with relevant literature; and signs a Risk Acknowledgement Form.
Ensure the women is on highly effective contraception (if necessary)
Ensure all women of childbearing potential on valproate are seen at least annually to re-valuate treatment, contraception (if necessary), discuss risks and sign an updated Risk Acknowledgement Form.

- Further details on the responsibilities of the specialist are given in the Guide for Healthcare professionals.

4. Ask the GP whether he or she is willing to participate in shared care and agree with the GP as to who will discuss the shared care arrangement with the patient

5. Periodically review the patient's condition and communicate promptly with the GP when treatment is changed. To review the patient and treatment at least once a year *until the patient is discharged from the mental health service where this is possible.*

6. Advise the GP on when to adjust the dose, stop treatment, or consult with the specialist.

7. Report serious adverse events to the MHRA and GP.

8. Ensure that clear back-up arrangements exist for GPs to obtain advice and support.

Baseline Tests
Liver function tests for valproate and carbamazepine

White blood cell and platelet counts for carbamazepine
Routine Tests

Liver function test for periodically for first 6 months for valproate and carbamazepine.
White cell counts if patient shows symptoms that cause concern

Disease monitoring
Please refer back to secondary care if patient deteriorates. With carbamazepine and lamotrigine monitor for suicidal ideation

Responsibilities of other prescribers

Acceptance of Responsibility by the Primary Care Clinician
It is optional for GPs to participate in taking on responsibility for shared care for the patient. GPs will take on shared care only if they are willing and able.

Summary

1. Reply to the request for shared care as soon as practicable.
2. Prescribe semisodium, sodium valproate, carbamazepine or lamotrigine at the dose recommended.
3. Adjust the dose as advised by the specialist.
4. To monitor physical parameters such as weight, fasting blood sugar, BP, smoking status and full lipid screen where necessary (at least annually).
5. For patients taking valproate – Ensure all women and girls who are of childbearing potential have been reviewed by a specialist in the last year and are on highly effective contraception. (Methods of contraception considered 'highly effective' in this context include the long-acting reversible contraceptives (LARC); copper intrauterine device (Cu-IUD); levonorgestrel intrauterine system (LNG-IUS); progestogen-only implant (IMP); and male and female sterilisation. These all have a failure rate of less than 1% with typical use. See guidance from FSRH for more information on user-independent methods and failure rates).
   Further details on the responsibilities of the GP are given in the Guide for Healthcare professionals.
6. To request earlier specialist review or seek specialist advice when necessary.
7. Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
8. Refer back to specialist if the patient's condition deteriorates, as advised.
9. Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
10. Report serious adverse events to the specialist and MHRA.

Clinical Particulars

BNF therapeutic class	**Valproate** Treatment of mania and hypomania (sodium valproate is licensed for epilepsy but is also used as a mood stabiliser) **Carbamazepine** prophylaxis of bipolar disorder unresponsive to lithium **Lamotrigine** is licensed for the prevention of depressive episodes in patients with bipolar I disorder who experience predominantly depressive episodes in people over 18 years of age
Cautions and Contraindications	**Valproate** Active liver disease Personal or family history of severe hepatic dysfunction, drug related Hypersensitivity to valproate semisodium or sodium or any other ingredient of the preparation. Porphyria Renal insufficiency may need to reduce dose **Carbamazepine** cardiac disease AV conduction abnormalities (unless paced); history of bone-marrow depression, acute porphyria, blood, hepatic or skin disorders **Lamotrigine** Parkinson's disease
Adverse Drug Reactions	Liver injury (see above) Nausea, GI disturbance diarrhoea Tremor, somnolence and confusion, headache Hyponatremia Anaemia and thrombocytopenia
Monitoring	Liver function tests for periodically for first 6 months of treatment (valproate carbamazepine and lamotrigine) WBC and platelet for carbamazepine
Interactions	▪ valproate semisodium or sodium may potentiate the effect of other psychotropics such as antipsychotics, MAO inhibitors, antidepressants and benzodiazepines ▪ valproate semisodium or sodium increases phenobarbital plasma concentrations ▪ valproate semisodium or sodium decreases phenytoin total plasma concentration ▪ Clinical toxicity has been reported when Depakote was administered with carbamazepine. ▪ The anticoagulant effect of warfarin and other coumarin anticoagulants may be increased following displacement from plasma protein binding sites by valproic acid. ▪ Plasma concentrations of carbamazepine increased by fluoxetine,diltiazem,and erythromycin ▪ Plasma concentrations of lamotrigine reduced by oestrogens ▪ Plasma concentrations of lamotrigine reduced by rifampicin

Communication

Specialist to GP
The specialist will inform the GP when they have initiated drug valproate semisodium or sodium, carbamazepine or lamotrigine. When the patient is near completing the satisfactory initiation period, the specialist will write to the GP to request they take over prescribing and where possible give an indication as to the expected length of treatment. The Specialist will also send a Shared care request form to support the GP in undertaking shared care. (Appendix A)

GP to specialist
If the GP has concerns over the prescribing of drug valproate semisodium sodium valporate, carbamazepine or lamotrogine, they will contact the specialist as soon as possible.

Contact names and details

Contact Details	Telephone number	Email
Kendray Pharmacy Team	01226 644338	kendraypharmacyteam@nhs.net
Dr S Chari (Early Intervention Team)	01226 644166	suresh.chari@swyt.nhs.uk
Dr A Karan (Core Team)	01226 645000	Anil.Karan@swyt.nhs.uk
Dr A Kandru (Enhanced East)	01226645001	Ankamma.Kandru@swyt.nhs.uk
Dr K Rele (Enhanced (West)	01226 644190	kiran.rele@swyt.nhs.uk

Development Process

This guidance has been produced by Sarah Hudson, Lead Pharmacist following an AMBER classification status of semisodium or sodium valproate carbamazepine or lamotrigine by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by the Area Prescribing Committee on 16th December 2020.

Appendix A – Shared Care request form (Amber)

- Specialist to complete when requesting GP to enter a shared care arrangement.
- GP to return signed copy of form.
- Both parties should retain a signed copy of the form in the patient's record.

From (**Specialist**): _____ **To** (**GP**): _____

Patient details

Name: _____ ID Number: _____

Address: _____ DOB: _____

Diagnosed condition: _____

Amber Drug details

Drug name: _____ Dose: _____

Date of initiation: _____ Length of treatment: _____

The patient will be reviewed by the Consultant on: _____

The patient should be reviewed by the GP by: _____

Monitoring

The following monitoring should be undertaken by the GP:

Parameter	Date next test due	Frequency
LFT		

Communication

Consultant
Telephone number: _____ Fax number:_____

Email address: _____

Specialist Nurse
Telephone number: _____ Fax number: _____

Email address: _____

Confirmation of acceptance of shared care

Specialist (Doctor/Nurse) name: _____

Specialist (Doctor/Nurse) signature: _____ Date: _____

I, Dr ……., can confirm I :

☐ accept the request to participate in shared care for the patient named above.

☐ reject the request to participate in shared care for the patient named above. The reason for this being ……..

GP signature: _____ Date: _____

To save resources you have been sent appendix A of the shared care document. The full document (Anticonvulsants as Mood Stabilisers Shared Care Guideline, *date approved December 2020*) can be accessed on the Barnsley BEST website at the following link:
http://best.barnsleyccg.nhs.uk/clinical-support/medicines/shared-care-guidelines/

Or via the Barnsley Area Formulary: http://www.barnsleyformulary.nhs.uk