BNSSG Health Community's Traffic Light System
Shared Care Guidance

Avon and Wiltshire NHS
Mental Health Partnership NHS Trust

Section 1: Heading

Trust(s)	**Avon and Wiltshire Mental Health Partnership NHS Trust**
	BNSSG Trusts
Speciality / Department:	Mental Health
Name of Medicinal Product and composition:	**Valproate semisodium (Depakote®) 250mg Tablets.** Containing 269.10mg of valproate semisodium* per tablet (equivalent to 250mg of valproic acid). **Valproate semisodium (Depakote®) 500mg Tablets**. Containing 538.20mg of valproate semisodium* per tablet (equivalent to 500mg of valproic acid). *Valproate semisodium is a stable coordination compound comprised of sodium valproate and valproic acid in a 1:1 molar relationship. It is also known as divalproex sodium (USAN). (1)
Indication	**It is prescribed for the treatment of manic episodes associated with bipolar disorder.** The continuation of treatment after manic episode could be considered in patients who have responded to valproic acid for acute mania (1) NICE recommends valproate as a first-line option for the treatment of acute episodes of mania, in combination with an antidepressant for the treatment of acute episodes of depression and for prophylaxis (3). **Valproic acid should not be routinely prescribed for women of child bearing potential**.

Date Approved March 2012

Date of Review March 2014

Section 2: Treatment Schedule

Please state the usual dosage range (the patient will have been stabilised, monitored on treatment and reviewed by the specialist). State also the formulation, frequency of administration and how long treatment should be continued and when the patient should be referred back to the specialist

Usual Dosage	<u>For adults (18 years and over)</u> • The initial recommended daily dose is 750 mg increased according to response (1). Clinical trials using a starting dose of 20mg valproate/kg body weight has also shown an acceptable safety profile (1). • The mean daily dose usually ranges between 1000mg and 2000mg valproate. (1) (2) • Patients receiving daily doses higher than 45mg/kg/day body weight should be carefully monitored. (1) (2)
Frequency of administration	Daily dosing given in 2 to 3 divided doses.(2)
Length of treatment	Continuation of treatment of manic episodes in bipolar disorder should be adapted individually using the lowest effective dose which produces the desired clinical effect. If treatment is stopped the dose should be reduced gradually over at least 4 weeks.
Referral back to specialist	• Renal and hepatic impairment – refer back for specialist advice – dosage adjustment necessary. • Pregnancy – valproates are known teratogens - refer back for specialist advice • Breast feeding- refer back for specialist advice

Section 3: Monitoring

Please give details of any tests that are required, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care) and cause for adjustment and when it is required to refer back to the specialist.

- People with bipolar have higher levels of physical morbidity and mortality than the general population (3). Weight gain can also be exacerbated by other drugs such as olanzapine and clozapine.(4).
- Secondary care to do physical health monitoring at baseline and at start of treatment.
- Primary care to do physical health monitoring at 6 months and as part of annual review -please see Table 1 page 3.
- Primary care to seek specialist advice from secondary care if results are abnormal.
- Additional periodic monitoring where appropriate - Increased liver enzymes are common, particularly at the beginning of therapy; they are also transient. Check FBC and INR before surgery.

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- Plasma levels to be done only in exceptional circumstances

Prescriber responsibilities:

Table 1

Test / measurement	Baseline	At start (1 month)	6months	Annual review
Thyroid function	✓			✓
Liver function	✓	✓	✓	✓
Renal function	✓			✓
Full Blood Count	✓	✓	✓	✓
Blood glucose (plasma)	✓			✓
Lipid profile	✓			Over 40s only
Blood pressure	✓			✓
Weight and height (BMI)	✓			✓
ECG	If indicated by history or clinical picture.			

Section 4: Side Effects

Please list the most common side effects and any management of them. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	***For a full list see manufacturer's summary of product characteristics*** **(SPC)** **www.medicines.org.uk** ***and also current BNF*** **Common** (> 10%) Sedation and weight gain. Gastrointestinal disorders (nausea, diarrhoea) frequently occur at the start of treatment and are often transient **Less common** (1-10%) dizziness, hair loss (usually remits in six months with possible curly re-growth). Transient asymptomatic elevations of hepatic enzymes have been seen occasionally, especially in early treatment. Menstrual disorders, ataxia and tremor are occasionally reported. Rarely photosensitivity and cutaneous reactions which may be severe. Severe liver damage, including hepatic failure sometimes resulting in fatalities, has been very rarely reported.
Referral back to specialist	• Report any serious, unacceptable or enduring adverse reactions to specialist • Any change in mood or development of suicidal thoughts likely to indicate a significant deterioration in the patients condition • Development of spontaneous bruising or bleeding

Section 5: Drug Interactions

Please list clinically significant drug interactions (see BNF appendix 1) and a reminder to ask the patients about particular problems

Significant Drug Interactions	• Antiepileptics - changes to metabolism and enhancement of toxicity reported. • Opioid analgesics – enhanced sedative and hypotensive effect • Olanzapine - higher risk of leucopenia and neutropenia when prescribed concomitantly. Weight gain can be exacerbated by other drugs that have this effect (e.g. antipsychotics, particularly clozapine and olanzapine). • Warfarin – enhanced anticoagulation. • Antidepressants - enhanced sedative and hypotensive effects. • Benzodiazepines – enhanced sedative effects. • Aspirin (Full dose) – shares Phase I metabolism with valproic acid and displaces valproic acid from plasma protein binding sites. Avoid concomitant prescribing except in prophylaxis (75-150mg).
Reminder to ask patients about particular problems	• Report any adverse reactions to GP and/or specialist. • Alert GP/specialist about any change in circumstances which could affect treatment (e.g. pregnancy or drug use). • Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge and if they have any queries regarding their condition and/or medication.

Section 6: Cautions and Special Recommendations

Please indicate the need to give or avoid specific treatment

Contra-Indication:

- Active liver disease
- Personal or family history of severe hepatic dysfunction, especially drug related
- Hypersensitivity to valproate or valproic acid
- Pancreatitis
- Porphyria

Section 7: Advice to the patient

Advice for GP/secondary care to pass onto the patient

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- Patients must inform the DVLA in the event of a manic episode and they are then advised to cease driving. They should also inform the DVLA about regular medication. It's a duty of the prescriber to ensure the patient is aware of this obligation. A patient whose mental state is stable may however drive safely (with the agreement of the DVLA) on valproate if they are not unduly sedated.
- Gradual discontinuation is generally recommended to avoid the risk of acute withdrawal syndromes or rapid relapse. If contemplating discontinuing at least 4 weeks tapering reducing dosage is recommended. If the patient stops the medication without medical advice please refer to the specialist psychiatrist.

Section 8: Responsibilities for Secondary Care

Please list the responsibilities of the secondary care team

- The patient will be involved in the choice of medication and verbal and written information will be provided by the specialist psychiatrist. The benefits and side effects of treatment will also be discussed with the patient.
- To assess the patient, establish the diagnosis and determine a care plan. Ensure care plan contains correct contact details for care co-ordinator/ key worker and specialist.
- To forward a care plan to the primary care prescriber
- To initiate therapy, arrange prescription and assess patient until stable.
- Discuss the proposal of shared care agreement with the patient. If possible obtain consent (verbal is fine) and document in notes. If patient declines SCA, then to please document this too.
- Ask the GP whether s/he is willing to participate in shared care. This must be done using the shared care agreement form for valproic acid (Depakote®).
- Ensure that the GP has a copy of the shared care agreement and a signed copy of the shared care agreement form.
- Prescribe the first 3 months of treatment of valproate semisodium..
- Ensure that arrangements of appropriate blood tests are made. Blood tests may be taken at the GP surgery providing appropriate communication with the GP and the GP is in agreement with this. Secondary care is responsible for the interpretation and monitoring of these blood test results for the first 3 months of treatment.
- Review results of any baseline tests and relay any abnormal findings to the GP with any appropriate advice.
- To review patient / provide advice as requested via the GP or Primary Care Liaison Service as necessary
- 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.
- To ensure the patient is fully informed about their treatment – for women of child bearing potential this should also include a discussion about plans for pregnancy and effective contraception as per NICE CG 38. Women who are trying to conceive and require valproate semi-sodium should be prescribed prophylactic folate.
- Patients on valproic acid, and their carers, should be advised how to recognise the signs and symptoms of blood and liver disorders and to seek immediate medical help if these develop.
- Discuss appropriate lifestyle issues e.g. healthy eating, with the patient.

- Monitor for response and adverse drug reactions; to report ADRs to MHRA & GP
- Communicate promptly with the GP when treatment is changed.
- Inform GP of concurrent therapy (as this may interact with other medication patient gets from GP)
- Advise the GP on when to adjust the dose, stop treatment (assuming no relapse in patients condition), or consult with the specialist.
- To ensure that prescribing outside of marketing authorisation is in line with best clinical practice
- Ensure that clear backup arrangements exist for GPs to obtain advice and support.

Section 9: Responsibilities for Primary Care
Please list the responsibilities of the GP

- Reply to the request for shared care within 3 weeks days of receipt of request.
- If the GP decides not to prescribe valproic acid, it should still be added to the patients repeat medication as a "non issued' item for information and safety purposes. The quantity should be set to *0 or 1. On the dose line it should read: *'Hospital prescribing only. Do not prescribe'*. This should also be done during the stabilisation period before GP takes over the prescribing (valproic acid is an enzyme inhibitor and may interact with other medication the patient is taking).
- To continue with prescribing after 3 months of treatment.
- To adjust dose / stop drug as advised by the specialist.
- To review the patient in accordance with an agreed care plan
- To monitor physical health parameters as per Section 3 where requested and feedback any clinically significant results to the specialist for advice.
- Inform specialist team of any change in patients medication that may interact with medication patient receives from secondary care.
- Monitor adverse effects such as sedation, tremor and gait disturbance in older people; report adverse effects to the specialist and MHRA.
- To request specialist review or seek specialist advice when necessary. (see ' Back-up advice and support for contact details)
- Once the patient has been discharged, advice may be sought from the Patient Care Liaison Service on any aspect of patients mental health that is of concern to the GP (see ' Back-up advice and support for contact details)
- To notify specialist of any relevant changes in other medications or clinical status.
- To ensure that practice staff are aware that valproate semi-sodium refers to Depakote® and not Epilim; caution when transcribing to patient medication records especially as have different license indications.

Section 10: Responsibilities of the Primary Care Liaison Service

- Accept referrals by registered GPs in line with DoH guidance.
- To advise the GP on appropriate action regarding any issues they may have on patients management regarding shared care.
- To try and resolve the issue(s) raised by the GP or to refer to the specialist team as appropriate.
- Rapid & Prioritised Specialist Mental Health Assessment with Recommendation/s for Care & Treatment within multiple care pathways.

- Determination of the nature & severity of mental health needs with consequent sign posting and pathway facilitation.
- Rapid and Accessible ongoing Support & Advice to the non-specialist workforce.
- Ongoing Education & Training for the non-specialist workforce.

Section 11: Contact Details

Name	Organisation	Telephone Number	E mail address	Fax
Specialist	AWP			
Bethan Shepherd, Formulary Pharmacist	AWP NHS Trust	07775562391	Bethan.shepherd@awp.nhs.uk	
Care co-ordinator				
Primary Care Liaison Service: BaNES	Intensive and Primary Care Liaison – Hillview Lodge	01225 371480		01225362799
Primary Care Liaison Service: Bristol	Intensive and Primary Care Liaison – interim to Speedwell then to Callington Road	0117 9195670		0117 9195625
Primary Care Liaison Service: North Somerset	Intensive and Primary Care Liaison – Long Fox Unit	01934 836406		01934 836405
Primary Care Liaison Service: South Gloucestershire:	Intensive and Primary Care Liaison – Bybrook Lodge, Blackberry Hill Hospital	01173 787960		0117 3787941
Primary Care Liaison Service: Swindon	Intensive and Primary Care Liaison –	01793 835787		01793 836817

	Sandalwood Court			
Primary Care Liaison Service: Wiltshire	Intensive and Primary Care Liaison – Green Lane and at Fountain Way	**North Wiltshire** (Green Lane Hospital): 01380 7311341 **South Wiltshire** (Fountain Way): 01722 820372		01380 731295 01380 731295

Section 11: Document Details

Date prepared	8th February 2012
Prepared by	S Mulvenna, updated by B Shepherd September 2012
Date of review	March 2014
Document Identification	SCP Valproic acid final 30.04.12 (V4)

Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

Section 13: References

Please list references

1. Electronic Medicines Compendium (www.medicines.org.uk), SPC for Depakote tablets accessed 08/02/2012
2. British Medical Association &Royal Pharmaceutical Society, British National Formulary 62, September 2011
3. NICE clinical guideline 38. Bipolar disorder July 2006.
4. Taylor D et al, Maudsely Prescribing Guidelines, 10th Edition