VALPROATE – PREFERRED PREPARATION for MENTAL HEALTH & LEARNING DISABILITY SERVICES

TARGET AUDIENCE	Nursing, medical and pharmacy staff working within Mental Health & Learning Disability services
PATIENT GROUP	All patients within NHS Lanarkshire Mental Health & Learning Disability services

Clinical Guidelines Summary

- Sodium valproate is the preferred valproate preparation for use in patients within NHS Lanarkshire's MHLD services.
- Sodium valproate is not directly equivalent to semisodium valproate.
- The use of gastro-resistant (enteric coated) formulations of sodium valproate minimises the risk of gastric side effects.
- Semisodium valproate is not included on the NHS Lanarkshire joint formulary
- Valproate must not be used in people of child-bearing potential unless there is a pregnancy prevention programme in place https://www.gov.uk/guidance/valproate-use-by-women-and-girls

Guideline Body

Scope

This policy is intended to provide guidance for the cost-effective and appropriate prescribing of valproate for **within all mental health and learning disability (MH&LD) settings in NHS Lanarkshire.**

Clinical judgement should be exercised on the applicability of any guideline, influenced by patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty. If there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

Background

NHS Lanarkshire's MH&LD Services have historically used 2 different valproate preparations - sodium valproate and valproate semisodium (Depakote®). The majority of sodium valproate formulations have a marketing authorisation (or product licence) for epilepsy[1], where as valproate semisodium has a licence for the treatment of manic episodes when lithium is contraindicated or not tolerated.[2] Valproate semisodium is only licensed for maintenance treatment of bipolar disorder if it was initially commenced for an acute manic episode.

Prior to the availability of valproate semisodium in the UK, sodium valproate was regularly used off-label as a mood stabiliser (out with the parameters of the marketing authorisation) and many prescribers continued to use sodium valproate in this way.

In 2010, the European Medicines Agency conducted a review of the safety of valproate in the treatment of manic episodes in bipolar disorder. The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of valproate in bipolar disorder outweigh their risks, and that all marketing authorisations for medicines containing valproate throughout Europe should be amended to include the treatment of manic episodes in bipolar disorders when lithium is contraindicated or not tolerated.[3] Despite this recommendation, the majority of sodium valproate preparations have not changed their marketing authorisations to include this as a licensed indication.

Sodium valproate is the preferred valproate salt within NHS Lanarkshire's MH&LD services and should be used in preference to valproate semisodium.

Commencing immediate release (gastro-resistant) sodium valproate	
Day 1 starting dose	200mg am & 400mg pm
Day 4	400mg twice daily
Day 7	500mg twice daily
Thereafter increase according to response and tolerability, aiming for between 1000-2500mg per day in 2 divided doses	

Switching from valproate semisodium to sodium valproate

Doses of valproate semisodium and sodium valproate are not directly equivalent.

- A 500mg valproate semisodium tablet contains the equivalent of 500mg valproic acid
- A 500mg sodium valproate tablet contains the equivalent of 433mg valproic acid [4]

Approximately 10- 15% higher dose of sodium valproate is required to take account of the extra sodium content.[4, 5] The doses below are practical suggestions for swapping valproate semisodium to an approximate equivalent dose of sodium valproate.

Valproate semisodium (Depakote®) total daily dose	Approximate equivalent sodium valproate total daily dose *	Suggested sodium valproate regime
500mg	600mg	**200mg am & 400mg pm** (200mg am and 2 x 200mg pm)
750mg	800mg	**400mg twice daily** (2 x 200mg am and pm)
1000mg	1200mg	**600mg twice daily** (3 x 200mg am and pm)
1250mg	1500mg	**500mg am + 1000mg pm** (500mg am and 2 x 500mg pm)
1500mg	1700mg	**700mg am + 1000mg pm** (500mg +200mg am and 2 x 500mg pm)
1750mg	2000mg	**1000mg twice daily** (2x500mg am and pm)
2000mg	2200mg	**1000mg am & 1200mg pm** (2 x 500mg am and 2 x 500mg + 200mg pm)

If there are tolerability issues with the switch from valproate semisodium to the approximate dose of sodium valproate, consider reducing the dose and gradually increasing to the approximate equivalent at a rate the patient can tolerate.
* 100mg crushable tablets of sodium valproate are available for dose adjustment but these are not enteric coated and therefore may be more likely to cause gastric disturbance (refer to *Further information and advice*)

Costs of treatment

Valproate semisodium is approximately 2 times the cost of an equivalent dose of immediate release (gastro-resistant) sodium valproate. Switching current valproate semisodium patients to an equivalent dose of immediate release (IR) sodium valproate would realise significant cost savings. Modified release (MR) preparations of sodium valproate that allow for once daily dosing are available. There are, however, little savings associated with a valproate semisodium to sodium valproate MR switch.

Further information and advice

- Both sodium valproate and valproate semisodium are metabolised to the pharmacologically active valproic acid.

- There is a perception that the use of valproate semisodium is better tolerated (especially with regards to gastric side effects) than equivalent doses of sodium valproate. The perceived better tolerability of semisodium over sodium valproate comes from US studies that compared enteric-coated (gastro-resistant) valproate semisodium with non-enteric coated valproic acid. [6,7] These findings do not extrapolate to valproate use in the UK where all solid forms of sodium valproate and valproate semisodium (with the exception of crushable 100mg tablets) are enteric coated (gastro-resistant).[4]

- Any gastric side effects that present can usually be overcome by taking valproate with or after food.

- Valproate semisodium is no longer included in the NHS Lanarkshire Joint Adult Formulary.[8]

- Valproate preparations **must not be used in any person of child-bearing potential** unless there is a pregnancy prevention programme in place. Refer to the MHRA's Valproate Guidance for full information. [9]

References/ Evidence

1. Epilim 500 Gastro-resistant tablets Summary of Product Characteristics. Last updated 15/08/22 www.medicines.org.uk accessed online 09/03/23

2. Depakote 500mg tablets Summary of Product Characteristics. Last updated 15/08/22 www.medicines.org.uk accessed online 09/3/23

3. European Commission decision on Valproate August 2010 https://www.ema.europa.eu/medicines/human/referrals/valproate

4. Fisher C, Broderick W. Sodium valproate or valproate semisodium: is there a difference in the treatment of bipolar disorder? Psych Bull 2003; 27:446-448

5. Taylor DM, Barnes TRE, Young AH. The Maudsley Prescribing Guidelines in Psychiatry. Wiley-Blackwell. 14th edition

6. Zarate CA, Tohen M, Narendran R, Tomassini EC, McDonald J, Sederer M, Madrid AR. The adverse effect profile and efficacy of divalproex sodium compared with valproic acid: a pharmacoepidemiology study. J Clin Psych 1999; 60:232-236

7. Brasfield KH. Pilot Study of divalproex sodium versus valproic acid: drug acquisition costs versus all related costs. Curr Ther Res 1999; 60(3): 138-144

8. NHS Lanarkshire Joint Adult Formulary. Joint Adult Formulary (scot.nhs.uk)

9. Medicines and Healthcare products Regulatory Agency. Guidance- Valproate use by women and girls. Last updated 11/2/21. Accessed online 9/3/23 https://www.gov.uk/guidance/valproate-use-by-women-and-girls

Appendix 1- Governance information for Guidance document

Lead Author(s):	Lorna Templeton & Jennifer Bryant Written originally for NHS GGC and adapted for use in NHS Lanarkshire
Endorsing Body:	Mental Health & Learning Disability Drug & Therapeutics Committee
Version Number:	2
Approval date	3rd May 2026 (originally Jun 2020)
Review Date:	May 2026

CONSULTATION AND DISTRIBUTION RECORD	
Contributing Author / Authors	• J Bryant, Advanced Clinical Pharmacist, Adult MH • L Templeton, Lead pharmacist, MHLD
Consultation Process / Stakeholders:	• Psychiatry • MHLD nursing • MHLD pharmacy
Distribution	• Dissemination to all MHLD, OAMH and CAMHS medical, nursing and pharmacy staff, wards and community teams • NHSL clinical guideline website and app

CHANGE RECORD		
Lead Author	**Change**	**Version No.**
L Templeton	New Guideline	1.0
J Bryant	Review. Update of references. Addition of scope Change of format in line with new CG template	2.0