Specialised Medicines Service Guideline ~ Sodium oxybate for narcolepsy with cataplexy in adults aged 19 and over

This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to SPC/data sheet for full prescribing data.

This guideline should be read in conjunction with the NEW Devon CCG commissioning policy for sodium oxybate for narcolepsy with cataplexy

Specialist: Please complete letter at the end of this document and send together with the guideline to the GP.

GP: Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.

GPs are invited to participate. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist

The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Introduction and aims of treatment

Sodium oxybate is a central nervous system depressant, licensed for the treatment of narcolepsy with cataplexy in adult patients.

Sodium oxybate is primarily considered as add-on therapy, for patients who receive inadequate benefit from stimulant medication such as methylphenidate, dexamfetamine, lisdexamfetamine, and modafinil; and antidepressants such as venlafaxine, clomipramine and other SSRIs.

This guideline refers to the use of sodium oxybate for the treatment of narcolepsy with cataplexy in adult patients, in line with the NEW Devon CCG commissioning policy. The use of sodium oxybate in patients who do not meet the **specified inclusion criteria**, or for other indications, is outside the scope of this guideline.

Specialist responsibilities

- Undertake pre-treatment assessment, monitoring & follow up as described in "Monitoring" below
- Discuss with the patient (and/or carer) the benefits, side effects, dosing schedule and monitoring requirements of sodium oxybate treatment; provide relevant supporting information in writing.
- For female patients of child-bearing age, exclude pregnancy prior to initiating treatment
- Discuss with the patient (and/or carer) the need to immediately consult their physician if there is a possibility of pregnancy
- Patients taking sodium oxybate will have an additional daily intake of sodium of 0.82 to 1.6 g (depending on dose). A dietary recommendation to reduce sodium intake should be considered in the management of patients with heart failure, hypertension or compromised renal function
- Warn patients against the use of any alcoholic beverages in conjunction with sodium oxybate

- Initiate treatment in line with commissioning criteria, including up-titration and stabilisation of dose, and assessment of efficacy (minimum 3 months)
- Assess efficacy (and eligibility for continuation) after 3 months' treatment in line with commissioning policy
- Send a letter to the GP, asking them whether they are willing to participate in the sharing of care for a particular patient. Include results of any relevant baseline tests
- Advise the GP (in writing) of any dose changes required
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed, including the current dose to be prescribed
- Provide any other advice or information for the GP if required.

General practitioner responsibilities

- Ensure a timely reply is sent to specialist in response to request for sharing of care.

If GP has agreed to share care:

- Undertake ongoing monitoring and act on results/reported side effects as described in "Monitoring" section below
- Continue to prescribe sodium oxybate in accordance with guidelines
- Report to and seek advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment
- Report adverse events to specialist and to MHRA via the yellow card scheme
- Stop treatment/amend dose in the case of a severe adverse event.

Monitoring

Assessment to be completed by the specialist service provider:

- Epworth Sleepiness Scale*, at baseline and after three months' treatment
- Cataplexy severity and frequency* (see commissioning policy), at baseline and after three months' treatment
- Blood pressure, at baseline and at first return assessment during initiation/up-titration.

*in order to assess efficacy, in line with criteria specified in the commissioning policy

Ongoing monitoring and action to be taken by the GP:

- Blood pressure, annually - If patient develops hypertension, seek specialist advice
- Adverse effects, at every contact.

Patient/carer responsibilities

- Ensure they attend specialist appointments and/ or GP/nurse appointments
- Understand that treatment may be stopped if they do not attend for monitoring & treatment review
- Ensure they have a clear understanding of the treatment, expected benefits and potential side effects
- Take (or support administration of) medication as directed by the prescriber
- Report any adverse effects regarding their treatment to the GP and/or specialist
- Advise the GP immediately if pregnancy is suspected
- Store their medicines safely and securely
- Patients with narcolepsy who hold a driving license must ensure the DVLA is aware of their diagnosis.

Supporting Information

Please refer to individual product SPCs for full prescribing data; these can be accessed at www.medicines.org.uk

Dosage and administration

Refer to the current BNF or individual product SPC for Xyrem oral solution.

Usual adult dose:

- Initially 2.25 g to be taken on retiring and 2.25 g after 2.5–4 hours, then increased in steps of 1.5 g daily in 2 divided doses, dose adjusted according to response at intervals of 1–2 weeks; dose titration should be repeated if restarting after interval of more than 14 days, maximum 9 g daily in 2 divided doses.

Patient specific guidance will be provided to the GP by the specialist.

Contraindications and precautions

Refer to individual product SPC for Xyrem oral solution.

Sodium oxybate is contraindicated in patients with major depression; patients with succinic semialdehyde dehydrogenase deficiency; and patients being treated with opioids or barbiturates.

Sodium oxybate has the potential to induce respiratory depression.

Special caution should be observed in patients with an underlying respiratory disorder.

Because of the higher risk of sleep apnoea, patients with a BMI ≥40 kg/m^2 should be monitored closely when taking sodium oxybate.

Sodium oxybate is considered to be unsafe in patients with porphyria.

All patients with impaired renal function should consider a dietary recommendation to reduce sodium intake.

The starting dose should be halved in all patients with hepatic impairment, and response to dose increments monitored closely.

Pregnancy and lactation

Refer to individual product SPC for Xyrem oral solution.

Animal studies have shown no evidence of teratogenicity but embryolethality was seen in both rat and rabbit studies.

Data from a limited number of pregnant women exposed in the first trimester indicate a possible increased risk of spontaneous abortions. To date no other relevant epidemiological data are available. Limited data from pregnant patients during second and third trimester indicate no malformative or foeto/neonatal toxicity of sodium oxybate.

Sodium oxybate is not recommended during pregnancy or breastfeeding.

Effects on ability to drive and use machines

Refer to individual product SPC for Xyrem oral solution.

Sodium oxybate has major influence on the ability to drive and use machines.

For at least 6 hours after taking sodium oxybate, patients must not undertake activities requiring complete mental alertness or motor co-ordination, such as operating machinery or driving.

When patients first start taking sodium oxybate, until they know whether this medicinal product will still have some carryover effect on them the next day, they should use extreme care while driving a car, operating heavy machines, or performing any other task that could be dangerous or require full mental alertness.

Patients with narcolepsy who hold a driving license must ensure the DVLA is aware of their diagnosis, for more information refer to https://www.gov.uk/narcolepsy-and-driving

Adverse effects

Refer to individual product SPC for Xyrem oral solution.

The most commonly reported adverse reactions are dizziness, nausea, and headache, all occurring in 10% to 20% of patients. The most serious adverse reactions are suicidal attempt, psychosis, respiratory depression and convulsion.

Abuse, misuse, and diversion

Sodium oxybate is the sodium salt of gamma hydroxybutyrate (GHB), and has well-known abuse potential. Prior to treatment physicians should evaluate patients for a history of or susceptibility to drug abuse. Patients should be routinely monitored and in the case of suspected abuse, treatment with sodium oxybate should be discontinued.

There have been case reports of dependence after illicit use of GHB at frequent repeated doses (18 to 250 g/day) in excess of the therapeutic dose range. Whilst there is no clear evidence of emergence of dependence in patients taking sodium oxybate at therapeutic doses, this possibility cannot be excluded.

Drug interactions

This list is not exhaustive, for additional information and further interactions, consult the BNF and individual product SPC for Xyrem oral solution.

- Sodium oxybate should not be used in combination with sedative hypnotics or other CNS depressants.
- The combined use of alcohol with sodium oxybate may result in potentiation of the CNS depressant effects of sodium oxybate, as well as increasing the risk of respiratory depression. Patients should be warned against the use of any alcoholic beverages in conjunction with sodium oxybate.
- There have been clinical observation(s) of coma and increased plasma GHB concentration after co-administration of sodium oxybate with topiramate. Therefore, patients should be warned against the use of topiramate in conjunction with sodium oxybate.

The following drug interactions are classified in the online version of the BNF as **potentially serious;** concomitant administration of the drugs involved should be **avoided** (or only undertaken with caution and appropriate monitoring).

- **Benzodiazepines:** effects of sodium oxybate enhanced by benzodiazepines (avoid concomitant use)
- **Opioid analgesics:** effects of sodium oxybate enhanced by opioid analgesics (avoid concomitant use)
- **Sodium valproate:** plasma concentration of sodium oxybate increased by sodium valproate (manufacturer advises reduce dose of sodium oxybate by 20%)
- **Valproic acid:** plasma concentration of sodium oxybate increased by valproic acid (manufacturer advises reduce dose of sodium oxybate by 20%).

Support

Contact details
Specific contact and support details will be provided to the GP by the specialist when requesting the sharing of care. Consultants can also be contacted via the individual trusts' switchboards: Northern Devon Healthcare NHS Trust: 01271 322577 Plymouth Hospitals NHS Trust: 01752 202082 Royal Devon and Exeter NHS Foundation Trust: 01392 411611

Date ratified: January 2018

Shared Care Agreement Letter - Consultant Request

To:	**Dr:**
	Practice Address:
Patient Name:	
NHS Number:	
Date of birth:	
Address:	

Diagnosed condition:..…….

I recommend treatment with the following drug: …….

At the following dosage: ……..……..

I request your agreement to continue the care of this patient according to the Specialised Medicines Service Guidelines for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate Specialised Medicines Service Guidelines.

The results of any relevant baseline tests and any additional supportive information (target range, date of last blood test etc.) are included below:

Principles:

GPs are invited to participate, but **if the GP is not confident to undertake these roles then they are under no obligation to do so.** If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Signed:			**Date:**
Consultant name:			
Telephone number:		**Fax number**	
Email address			

Please sign below and return promptly. Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

GP Response

I agree / do not agree* to share the care of this patient in accordance with the Specialised Medicines Guideline.

Signed: …….. Date: …….

GP name: …… *Delete as appropriate.

Patient agreement

I understand and agree to my responsibilities as described above.

Signed: …….. Date: …….

Name: