SHARED CARE PRESCRIBING GUIDELINE
SODIUM OXYBATE

DOCUMENT DETAILS

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Comments on this document to:	Clinical Governance Pharmacist c/o Pharmacy Department, Guy's Hospital

CHANGE HISTORY

Date	Change details	Approved by
June 2011	Changes made based on feedback from Lambeth PCT	

Sodium Oxybate▼

TREATMENT OF CATAPLEXY IN ADULT PATIENTS WITH NARCOLEPSY

NOTES to the GP

The information in the shared care guideline has been developed in consultation with Primary Care and it has been agreed that it is suitable for shared care.
This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing this drug.

The questions below will help you confirm this:

- Is the patient's condition predictable or stable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.
If the answer is NO to any of these questions you should contact the requesting consultant or your local PCT medicines management team. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Prescribing should follow requirements in the South East London Interface Prescribing Policy
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount

Date shared care guideline prepared: July 2008 then updated Aug 2010 **Approved by:** Medicines Management Committee. Lambeth & Southwark PCT 31 Oct 2011 **Approved by DTC :** GSTFT 10 Nov 2011 **Review date:** Nov 2013	**Prepared by:** Dr Chris Kosky (Consultant Physician, Sleep Centre) Gráinne d'Ancona (Principal Pharmacist, Acute Medicine)

REQUEST FOR SHARED CARE

Consultant Name:	**Patient name:**
Consultant signature:	**Hospital Number:** **NHS Number:**
Date completed:	**D.O.B**
GP Name	**Diagnosis/Indication**

ACTION

HOSPITAL:

- Email/Fax completed shared care guideline to GP for attention and action
- F**ax details for GPs** can be found **www.nhs.uk/**
- Original to be filed in Patient's clinical record

GP PRACTICE:

- Please consider request within 2 weeks
- If named GP is not available over the next week pass request to a GP colleague.
- **If agree** to request initiate prescribing as detailed in shared care guideline. Confirmation to the requesting consultant is not required, it will be assumed after 2 weeks.
- **If do not agree** to request contact consultant or local PCT medicines management team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the local PCT Medicines Management team should be informed.
- Once decision reached file copy in patient's notes.

Attach patient addressograph

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This medicine is monitored intensively by the CHM and MHRA. Detailed information is available on the website of the European Medicines Agency http://www.ema.europa.eu/

1. CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the consultant and the GP are in agreement that the patient's condition is stable or predictable.
- The hospital will provide the patient with a supply of therapy until the patient is stable.

2. AREAS OF RESPONSIBILITY

Consultant	GP
▪ Establish or confirm diagnosis and assess patient suitability for treatment ▪ Baseline monitoring ▪ Epworth Sleepiness score ▪ Discuss treatment with patient and ensure they have a clear understanding of it. http://www.medicines.org.uk/EMC/medicine/17365/PIL/Xyrem%20500%20mg%20ml%20oral%20solution/ ▪ Email/Fax a signed shared care guideline with patient details completed to GP for consideration of shared care request ▪ Initiate treatment and provide a minimum of 2 weeks supply to the patient. ▪ Prescribe and monitor treatment according to local guideline or formulary until patient's condition is stable or predictable ▪ Sodium oxybate, which is as the sodium salt of Gabba hydroxyl-butyrate, is a CNS depressant active substance with well known abuse potential.However the incidence of abuse with sodium oxybate is extremely low amongst treated patients with narcolepsy. Physicians will evaluate patients for a history of drug abuse and follow such patients closely *After agreement to shared care* ▪ Inform GP when patient is stable ▪ Inform GP of abnormal monitoring results and any changes in therapy ▪ Evaluate adverse events reported by GP or patient ▪ Carry out ongoing monitoring and follow up accordingly to shared care guidelines including continued need for therapy.	▪ Consider shared care proposal within 2 weeks of receipt ▪ If agreement to shared care take over prescribing responsibility. Confirmation to the requesting consultant is not required, it will be assumed after 2 weeks. ▪ If do not agree to shared care discuss with requesting consultant or local PCT medicines management team within 2 weeks of receipt of shared care request *After agreement to shared care* ▪ Prescribe dose as recommended once the patient's condition is stable or predictable ▪ Monitor general health of patient and check adverse effects as appropriate ▪ Inform specialist consultant of suspected adverse effects and also report via yellow card scheme if necessary ▪ Stop treatment on advice of specialist or immediately if urgent need arises ▪ Check compatibility interactions when prescribing new or stopping existing medication ▪ Carry out monitoring and follow up according to shared care guideline ▪ Discuss any abnormal results with specialist consultant and agree any action required ▪ Only ask specialist to take back prescribing should unmanageable problems arise. Allow an adequate notice period ▪ General Practitioners should monitor patients for evidence of drug misuse and inform the named consultant of their concern.

3. PATIENTS RESPONSIBILITIES (add specific additional responsibilities where applicable)

- Take medicines as agreed
- Report any adverse effects to GP or hospital doctor
- Do not share medicines
- While this product does not require any special storage conditions, it should be kept safely out of reach and sight

4. COMMUNICATION AND SUPPORT

Hospital contacts:

SLEEP DISORDERS CENTRE
St. Thomas's Hospital, Lambeth Palace Road, SE1 7EH
Tel: 0207 188 8937
Fax: 0207 188 6114

Specialist Consultant physicians :
Prof Adrian Williams:
Adrian.Williams@gstt.nhs.uk
Dr Chris Kosky:
Chris.Kosky@gstt.nhs.uk
Dr Rexford Muza:
Rexford.Muza@gstt.nhs.uk
Dr Guy Leschziner;
Guy.Leschziner@gstt.nhs.uk
Dr Joerg Steier
Joerg.Steier@gstt.nhs.uk

Attach patient addressograph

Sodium Oxybate▼

5. CLINICAL INFORMATION

Indication(s):	Licensed indication: Treatment of narcolepsy with cataplexy in adult patients
Place in Therapy:	See appendix 1. Briefly sodium oxybate is used in narcolepsy for severe, resistant and disabling cataplexy were other agents have failed, are poorly tolerated or are contraindicated. Occasionally, it may be used for severe sleepiness in patients with narcolepsy where stimulant therapy has failed, is poorly tolerated or is contraindicated.
Dose & route of administration:	• The recommended starting dose is 4.5 g/day sodium oxybate (9 ml Xyrem®) divided into two equal doses of 2.25 g/dose (4.5 ml/dose). The dose should be titrated to effect based on efficacy and tolerability up to a maximum of 9 g/day divided into two equal doses of 4.5g/dose (9ml/dose) by adjusting up or down in dose increments of 1.5 g/day (i.e. 0.75 g/dose or 1.5 ml/dose). A minimum of two weeks is recommended between dosage increments. • Each dose of Xyrem® must be diluted with 60 ml of water in the dosing cup prior to ingestion. Single doses of 4.5g should not be given unless the patient has been titrated previously to that dose level. • Because food significantly reduces the bioavailability of sodium oxybate, patients should eat at least several (2-3) hours before

	taking the first dose of Xyrem® at bedtime. Patients should always observe the same timing of dosing in relation to meals. Xyrem® should be taken orally upon getting into bed and again between 2.5 to 4 hours later. • ***Discontinuation of Xyrem®:*** The discontinuation effects of sodium oxybate have not been systematically evaluated in controlled clinical trials. If the patient stops medication for more than 14 consecutive days, titration should be restarted as per initiation regimen • ***Patients with hepatic impairment:*** The starting dose should be halved in patients with hepatic impairment, and response to dose increments monitored closely • ***Patients with renal impairment:*** Patients with impaired renal function should consider a dietary recommendation to reduce sodium intake • ***Elderly patients:*** Elderly patients should be monitored closely for impaired motor and/or cognitive function when taking sodium oxybate
Duration of treatment	Lifelong, if effective and tolerated
Criteria for stopping treatment	▪ Significant adverse drug reaction ▪ Lack of efficacy ▪ At request of patient
Monitoring Requirements including frequency:	**Consultant:** Epworth Sleepiness Score is reviewed at each clinic visit **GP:** Adverse reactions and inform the name consultant if concerns that the patient maybe abusing the medication.
Follow up arrangements	**Consultant**: every 3 months for one year, then every 6 months **GP**: Nil specific required
Practical issues including other relevant advice/information:	See appendix 1.
Information provided	See appendix 1.
Evidence Base for treatment and Key references:	▪ Trial data and clinical evaluation available on request from GSTFT JFC ▪ http://www.medicines.org.uk/EMC/medicine/17364/SPC/Xyrem+500+mg+ml+oral+solution/

NB: for full details of adverse effects and drug interactions refer to latest Summary of Product Characteristics

Appendix 1. Background to the condition and management

As yet there is no cure for narcolepsy, a debilitating sleepiness condition which, though not life-limiting, is life-altering. Treatment is directed at the two main symptoms of the condition on the one hand sleepiness and on the other hand phenomena usually associated with dreaming sleep but present in wakefulness, specifically cataplexy, (sudden temporary paralysis associated with emotions such as laughter, anger or fright), sleep paralysis and sleep-onset dreams or hallucinations.

What is cataplexy?

When present, this may be a minor inconvenience with trivial localised paralysis or total collapse. Treatment is needed in two-thirds of patients. The most common agent used is Clomipramine, a tricyclic antidepressant which is effective to a degree, but associated in particular with weight gain and drowsiness (if used in the day). Also urinary retention, blurred vision, dry mouth and sometimes impotence can also occur. More physicians however now recommend one of the SSRIs which do not in general have these side effects but others including poor sleep. There is a concern about the long term effects of these drugs, being taken for a non-approved indication and for much longer than usual.

To date there has been no approved treatment for the serious and debilitating symptom of cataplexy which, untreated, is associated as previously described, with significant physical and psychological morbidity. Substantial evidence exists suggesting that, without effective treatment, narcoleptics attempt to manage their cataplexy by controlling or suppressing their emotions (adopting a flat affect) or simply avoiding social or other occasions. As a result they may be mislabelled as bored, disinterested or unintelligent. Thus, there is a profound need to treat this poorly understood symptom, and of course to treat with approved agents that are free of important side effects.

Sodium oxybate has been shown to significantly reduce cataplexy within four weeks, with near abolition within six months and is the first approved treatment for cataplexy. It also reduces sleepiness and improves nocturnal sleep.

Users need a more effective and approved medication, to replace the off-label use of REM sleep-suppressing antidepressants. While some patients report relief from cataplexy with these drugs, tolerance to their beneficial effects may occur and it is of concern that their sudden withdrawal may precipitate a marked increase in the number and severity of cataplexy attacks (in its most severe form, known as status cataplexicus). Sodium oxybate does not have this disadvantage.

Special Warnings or Precautions for Use

- Sodium oxybate has the potential to induce respiratory depression.
- Sodium oxybate is the salt of GHB, a CNS depressant with abuse potential. There have been case reports of dependence after illicit use of GHB at frequent repeated doses (18-250g/day).While there is no evidence of dependency in patients taking sodium oxybate at therapeutic doses, this possibility cannot be excluded.
- The combined use of alcohol or any CNS depressant drug with sodium oxybate may result in potentiation of the CNS-depressant effects of sodium oxybate. Therefore, patients should be warned against the use of alcohol in conjunction with sodium oxybate.
- Sodium oxybate is considered to be unsafe in patients with porphyria.
- Sodium oxybate also has the potential to induce respiratory depression. Patients should be questioned regarding signs of CNS or respiratory depression. Special caution should be observed in patients with an underlying respiratory disorder.
- The concomitant use of benzodiazepines and sodium oxybate should be avoided due to increased risk of respiratory depression
- Sodium oxybate may cause confusion; other neuropsychiatric events include psychosis, paranoia, hallucinations, and agitation. The emergence of thought disorders and/or behavioural abnormalities when patients are treated with sodium oxybate requires careful and immediate evaluation. The emergence of depression when patients are treated with sodium oxybate requires careful and immediate evaluation. Patients with a previous history of a depressive illness and/or suicide attempt should be monitored especially carefully for the emergence of depressive symptoms while taking sodium oxybate.
- If a patient experiences urinary or faecal incontinence during sodium oxybate therapy, the prescriber should consider pursuing investigations to rule out underlying aetiologies.
- Sleepwalking has been reported in patients treated in clinical trials with sodium oxybate.

- Patients taking Xyrem® will have an additional daily intake of sodium that ranges from 0.75g (for a 4.5g/day (9ml) Xyrem® dose) to 1.6g (for a 9g/day (18ml) Xyrem® dose). A dietary recommendation to reduce sodium intake should be carefully considered in the management of patients with heart failure, hypertension or compromised renal function.
- Patients with compromised liver function will have an increased elimination half-life and systemic exposure to sodium oxybate. The starting dose should therefore be halved in such patients, and response to dose increments monitored closely.
- Elderly patients should be monitored closely for impaired motor and/or cognitive function when taking sodium oxybate.
- Sodium oxybate is not recommended in patients under 18 years of age is not recommended.
- Sodium oxybate is not recommended in patients with epilepsy.
- In some patients, cataplexy may return at a higher frequency on cessation of sodium oxybate therapy, however this may be due to the normal variability of the disease. In rare cases, events such as insomnia, headache, anxiety, dizziness, sleep disorder, somnolence, hallucination, and psychotic disorders were observed after GHB discontinuation.

Storage

Sodium oxybate comes in a bottle with two containers for mixing the medication. Both the bottle and storage containers have child proofed caps. The mixed solution should be kept in a bed side draw just before going to sleep. If there are children in the house, this draw should be locked or be out the reach of children.

Pregnancy and Lactation

- Not recommended during pregnancy.
- Breast-feeding is not recommended when using Sodium Oxybate.

Narcolepsy and Driving

The patient is obligated by law to notify the Driver and Vehicle Licensing Agency (DVLA) of the diagnosis of Narcolepsy. Group one licence holders (car, motorbike) must cease driving on the diagnosis of the narcolepsy. Driving will be permitted when satisfactory control of symptoms is achieved, then 1, 2 or 3 year licence with medical review, till 70 years of age. Licence restored after 7 years of satisfactory control. Group two licence holders (LGV/PCV) are generally considered unfit to drive this class of vehicle permanently. However, if a long period of symptom control has been established, licensing may be considered on a individual basis.

Effects on Ability to Drive and use Machines

- Sodium oxybate has a major effect on the ability to drive and use machines. These patients should already be known to the DVLA
- For at least 6 hours after taking sodium oxybate, patients must not undertake activities requiring complete mental alertness or motor coordination, such as operating machinery or driving.
- When patients first start taking sodium oxybate, they should take extreme care when driving, operating heavy machines or performing any other task which is dangerous or requires full mental alertness.

Contraindications

- Hypersensitivity to sodium oxybate or to any of the excipients.
- Patients with succinic semialdehyde dehydrogenase deficiency.
- Patients being treated with opiates or barbiturates.

Interactions

- The combined use of alcohol with sodium oxybate may result in potentiation of the central nervous system-depressant effects of sodium oxybate.
- Sodium oxybate should not be used in combination with sedative hypnotics or other CNS depressants.
- Since sodium oxybate is metabolised by GHB dehydrogenase there is a potential risk of an interaction with drugs that stimulate or inhibit this enzyme (e.g. valproate, phenytoin or ethosuximide). No interaction studies have been conducted in human subjects.
- Possible additive effect of antidepressants and sodium oxybate cannot be excluded. The rates of adverse events are increased when sodium oxybate is co-administered with tricyclic antidepressants.