Protocol for the Management of Patients Receiving Sodium Oxybate for Narcolepsy

Key points of this document

- Outlines process for supply of sodium oxybate for narcolepsy in the East of England Region.
- Provides supporting guidance for both tertiary care and primary care practitioners.

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1. Prescribing Guidance

- **Indication:** Sodium oxybate is licensed for the treatment of narcolepsy in adult patients with cataplexy.
- **Prescribing Restrictions:** A **Hospital Only Medicine** initiated by a Consultant Sleep Physician for patients with a definitive diagnosis of narcolepsy with cataplexy in whom all other suitable treatment options have failed to improve symptoms.
  The Specialist Sleep Centre is responsible for ongoing management of patients requiring sodium oxybate. Supply of sodium oxybate is made via monthly FP10(HP) prescriptions written by the Specialist Team and sent to the patient's nominated Community Pharmacy for dispensing.
  This is a schedule 2 Controlled Drug and the associated prescription requirements of the Misuse of Drugs Act must be met.
- **Dose:** Initially 2.25g on retiring and repeated 2.5 to 4 hours later, usually increased in steps of 1.5g daily in two divided doses at intervals of 2 weeks; usual maximum 9g daily in two divided doses.
- Initiation of sodium oxybate will be communicated to the GP Practice by the Pharmacy Homecare Team for inclusion in the Summary Care Record (SCR). *See appendix 1 for letter template.*
- **Monitoring:** Efficacy and blood-pressure monitoring to be carried out by Specialist Centre on a 6-monthly basis. No blood test monitoring is required for this medication.
- **Stopping Treatment:** If, after a trial period (usually 8 weeks), a patient fails to tolerate or respond to sodium oxybate therapy it will be stopped by the Specialist. The Specialist will also stop therapy if the clinical picture changes and it is no longer considered suitable. This will be communicated to the GP Practice to enable the SCR to be updated accordingly.

2. Supply Process

1. Specialist provides patient with information on the supply arrangements including expectations that they will:
   a. Attend scheduled outpatient review appointments.
   b. Share any concerns they have about their treatment with the Sleep Centre.
   c. Nominate a Community Pharmacy to collect their medication from on a monthly basis.
   d. Take their medication as per the prescription and in accordance with the additional medication-specific instructions on the patient information leaflet contained within the box.
   e. Dispose of any excess medication by returning it to the nominated Community Pharmacy.
2. Specialist notifies Homecare Team of new patient and patient's preferred Community Pharmacy by email to Pharmacy Home Care.

3. Homecare Team contacts nominated Community Pharmacy and obtains their agreement to participate in the scheme. Arrangements are made to send monthly FP10 prescriptions for dispensing (sufficient controlled drug storage capacity should be confirmed).
4. Homecare team will send letter to GP Surgery to inform them that patient is receiving sodium oxybate from the Hospital and request this information is entered onto the Summary Care Record.
5. At regular intervals, Homecare Team will request FP10 prescriptions from Specialist, and email Community Pharmacy when they are sent out.
6. Royal Mail Special Delivery will be used until such a time as electronic transfer of prescriptions is available.
7. Community Pharmacy will be asked to email back a copy of the enclosed *sodium oxybate prescription receipt confirmation slip* to confirm receipt of prescription. *See appendix 2 for letter template.*
8. Records of prescriptions sent for patients on the sodium oxybate homecare supply scheme will be kept in the Shared folder: Narcolepsy medication supplies.
9. Continued 2-way communication between the Homecare Team and the Community Pharmacist throughout the lifetime of the agreement is essential.

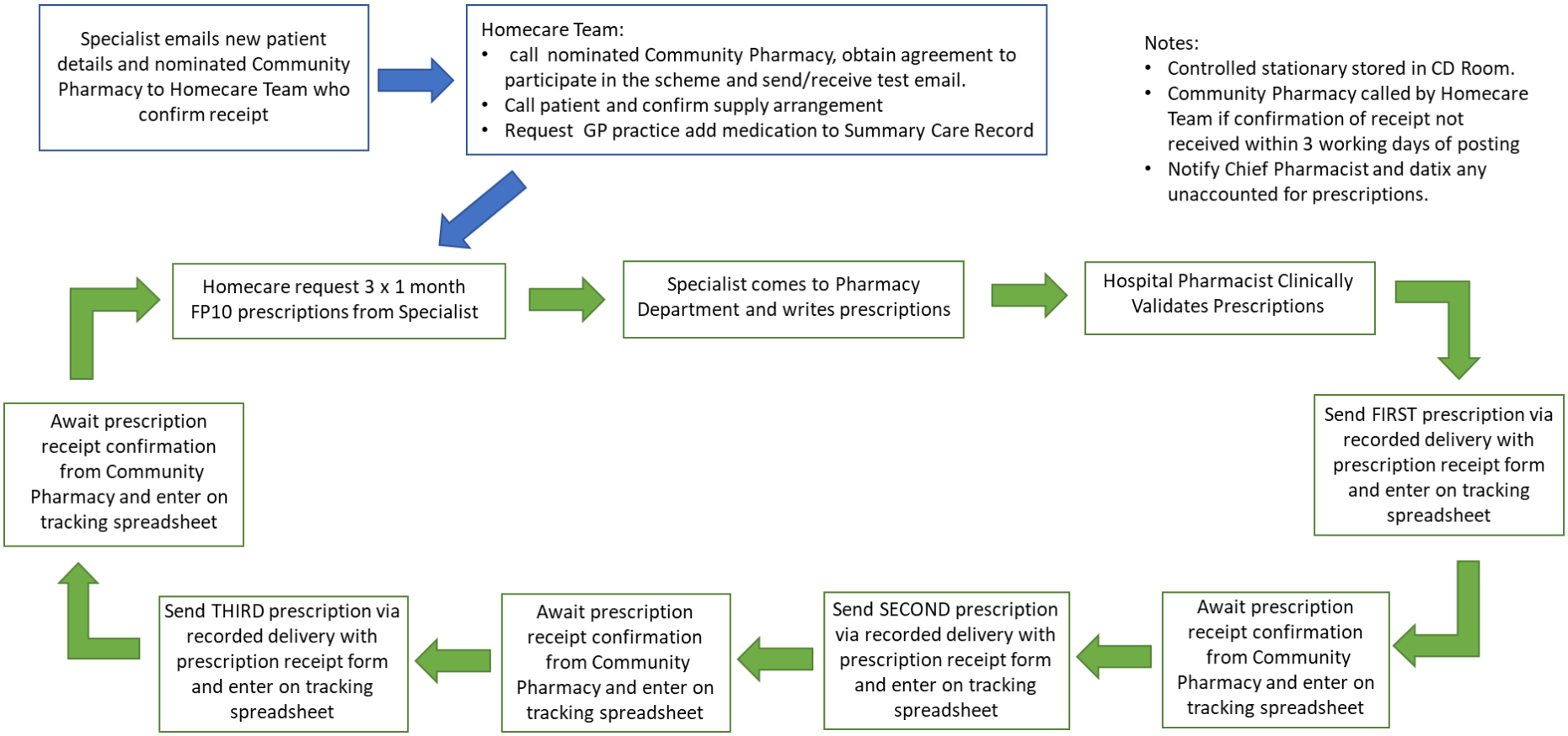
Note: When devising this unique method of managing maintenance supplies of sodium oxybate other, more conventional, avenues were explored but rejected:

Ideally supply would be made via a homecare delivery service but, as these companies are not set up to deliver high volume liquid formulations of schedule 2 controlled drugs, this is not currently an option.

It is not good practice to make regular deliveries of controlled drugs via Royal Mail or private courier companies.

It is not reasonable to expect all patients will be able to make the journey to Royal Papworth Hospital each month to collect their medication in person, and making larger supplies of a schedule 2 CD is not recommended.

3. Prescription Processing Flowchart for Sodium Oxybate



4. Key Contacts

Patients and General Practitioners are encouraged to contact the Specialist in the first instance. Community Pharmacists are encouraged to contact the Pharmacy Homecare Team in the first instance.

Royal Papworth Hospital NHS Foundation Trust

(Respiratory Support and Sleep Centre (RSSC) -Tertiary referral centre)

Specialist	Post	Telephone (direct line)
Dr Ian E Smith	Medical Director of Royal Papworth Hospital and Consultant Sleep Physician	01223 639715
Dr Tim Quinnell	Consultant Sleep Physician	01223 639718
Dr Mike Davies	Consultant Sleep Physician	01223 638571
Dr Nick Oscroft	Consultant Sleep Physician	01223 639803
Dr M Mason	Consultant Sleep Physician	01223 638401
Dr D Wozniak	Consultant Sleep Physician	01223 639619
Mr Duncan Grady	Lead Pharmacist	01223 638700
Mr Richard Chapple	Principal Pharmacy Technician Homecare Services	01223 638540 phn-tr.pharmacyhomecare@nhs.net
Pharmacy Medicines Helpline	Non-urgent Medicines Information for patients receiving sodium oxybate from Royal Papworth Hospital	01223 638777 (answerphone)

5. FP10 Prescription Writing Guidance for Consultant Sleep Physicians

Prescriptions must meet the legal requirements for a Schedule 2 drug. For example:

- **Write or print** the name and address of the patient *(addressograph labels not permitted)*
- Sodium Oxybate 500mg/mL Oral Solution *(drug, strength and form)*
- 2.25grams at bedtime and 2.25grams 2.5 – 4 hours later *('to be taken as directed' not permitted)*
- Supply 360 (three hundred and sixty) millilitres *(total quantity in words and figures, no abbreviations)*
- Hand signed by prescriber *(digital signature not permitted)*
- Prescriptions may be post-dated *(supply can only be made within 28 days of the date)*
- **Dr** Sleep *(Must include your designation)*
  Royal Papworth Hospital NHS Foundation Trust
  Papworth Road
  Cambridge Biomedical Campus
  Cambridge, CB2 0AY

6. Clinical Considerations for Primary Care Practitioners

Mechanism of Action:

Sodium oxybate is a central nervous system depressant which reduces excessive daytime sleepiness and cataplexy and modifies sleep architecture, reducing fragmentation of night-time sleep. The use of sodium oxybate is associated with dose-related improvements in the symptoms of narcolepsy and reduction in the frequency of cataplexy attacks.

The precise mechanism by which sodium oxybate produces an effect is unknown, however it is thought to act by promoting slow (delta) wave sleep and consolidating night-time sleep. Administration before nocturnal sleep increases Stages 3 sleep and increases mean sleep latency on daytime naps tests, whilst reducing the frequency of sleep onset REM periods (SOREMPs).

In the clinical trial database, greater than 80% of patients maintained concomitant stimulant use with agents such as modafinil, methylphenidate or dexamfetamine.

Sodium oxybate is a sodium salt of gamma hydroxybutyrate (GHB), a CNS active substance with well-known abuse potential. During treatment, patients should be monitored for the risk of diversion, misuse and abuse of sodium oxybate.

Potential to Induce Sleep Apnoea:

Sleep apnoea occurs in up to 50% of patients with narcolepsy. Sodium oxybate also has the potential to induce sleep apnoea.

Patients are assessed before treatment for any underlying respiratory disorder and caution should be exercised when considering treatment in these patients.

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

Dose Range:

Sodium oxybate is required to be taken at bedtime while in bed and again 2.5 to 4 hours later. The recommended starting dose is 4.5g/day divided in two equal doses of 2.25g. The starting dosage can then be increased to a maximum of 9g/day, in increments of up to 1.5g/day (i.e. 0.75g per dose). A minimum of one to two weeks is recommended between dosage increases to evaluate clinical response and minimize adverse effects. The dose of 9g/day should not be exceeded. If the patient stops taking sodium oxybate for more than 14 days then titration should be restarted from the lowest dose.

Administration:

Absorption is delayed and decreased by a high fat meal and the patient should be told to eat at least 2 to 3 hours before taking the first dose of sodium oxybate. Patients should try to minimise variability in the timing of dosing in relation to meals.

Both doses of sodium oxybate should be prepared prior to bedtime. Each dose must be diluted with 60mls of water in the child resistant dosing cups provided prior to ingestion. Patients will probably need to set an alarm to awaken for the second dose. After ingesting each dose patients should then lie down and remain in bed.

After dilution in the dosing cups, the preparation should be used within 24 hours. Each Sodium Oxybate bottle should be discarded 40 days after opening.

Hepatic and renal impairment:

The doses should be halved in patients with compromised liver function and dose increments monitored closely. Sodium Oxybate is metabolised in the liver to inactive metabolites and clearance is almost entirely by biotransformation to carbon dioxide, which is then eliminated by expiration.

As less than 5% is excreted via the kidney no dosage adjustment should be necessary in patients with renal impairment. The high sodium content of sodium oxybate should be taken into consideration in patients with impaired renal function.

Sodium Intake:

Daily sodium intake in patients taking sodium oxybate ranges from 0.5g (for a 3g dose) to 1.6g (for a 9g dose). The recommended maximum dietary intake of sodium is 2.4g per day. A dietary recommendation to reduce sodium intake should be carefully considered in patients with heart failure, hypertension or compromised renal function.

Dosing in the Elderly:

Elderly patients should be monitored closely for impaired motor and/or cognitive function when taking sodium oxybate.

Neuropsychiatric events:

Patients may become confused while being treated with sodium oxybate. If this occurs, they should be evaluated fully, and appropriate intervention considered on an individual basis.

Other neuropsychiatric events include anxiety, psychosis, paranoia, hallucinations, and agitation. The emergence of thought disorders including thoughts of committing violent acts (including harming others) and/or behavioural abnormalities 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 affective disorders (including depressive illness, anxiety and bipolar disorder), suicide attempt and psychosis should be monitored especially carefully for the emergence of depressive symptoms and/or suicidal ideation.

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 with sodium oxybate. The risk of injury or self-harm should be borne in mind in any patient with sleepwalking. Therefore, episodes of sleepwalking should be fully evaluated and appropriate interventions considered.

Effects on ability to drive and use machines:

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.

Clinically Significant Drug Interactions:

Increased sodium oxybate levels when administered with GHB dehydrogenase inhibitors. For patients taking valproate (a GHB dehydrogenase inhibitor), a decrease in sodium oxybate dose by 20% is recommended. The recommended starting dose for sodium oxybate is 3.6 g per day administered orally in two equal divided doses of approximately 1.8 g. The use of topirimate is contra-indicated (see below).

Cumulative CNS depressant effects when administered with other CNS-depressant medicines. There is also a significant increased risk of respiratory depression. Some CNS depressants are contra-indicted (see below).

Contraindications:

Benzodiazepines, opioids or barbiturates - cumulative effect on respiratory depression.
Alcohol - The potentiation of the central nervous system-depressant effects of sodium oxybate. Patients should be warned against the use of any alcoholic beverages in conjunction with sodium oxybate.
Topirimate - 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.

Epilepsy - Seizures have been observed in patients treated with sodium oxybate. In patients with epilepsy, the safety and efficacy of sodium oxybate has not been established, therefore use is not recommended.
Major depression – increased risk of suicide ideation.
Porphyria – clinical trials demonstrated porphyrogenic effects.
Succinic semialdehyde dehydrogenase deficiency.
Pregnancy and Breastfeeding – due to lack of safety data.

Adverse Effects

Very common (≥ 1 in 10)

- dizziness
- headache
- nausea (the frequency of nausea is higher in women than men)

Common (≥ 1 in 100 and < 1 in 10)

- blood pressure increase
- weight decrease
- feeling drunk
- hyperhidrosis
- enuresis nocturna
- nasopharyngitis and sinusitis
- depression

Uncommon (≥ 1 in 1000 and < 1 in 100)

- initial insomnia
- hypersensitivity
- agitation, abnormal thinking, paranoia, hallucination, psychosis, suicide

Further information can be found in the **Summary of Product Characteristics.**

Withdrawal:

No withdrawal effects have been seen with Sodium Oxybate at therapeutic doses. Trials have shown acute withdrawal led to a gradual increase in the number of cataplexy attacks.

Overdose:

In an emergency, healthcare professionals should call the 24hr National Poisons Information Service on 0344 892 0111.

Patients have exhibited varying degrees of depressed consciousness that may fluctuate rapidly between a confusional, agitated combative state with ataxia and coma.

Due to the rapid metabolism of sodium oxybate supportive measures are usually sufficient.

Emesis (even with impaired consciousness) has been observed. Therefore appropriate posture (left lateral recumbent position) and protection of the airway by intubation may be warranted. Although gag reflex may be absent in deeply comatose patients, even unconscious patients may become combative to intubation, and rapid sequence induction (without the use of sedative) should be considered.

Bradycardia and hypothermia may accompany unconsciousness, as well as muscular hypotonia, but tendon reflexes remain intact. Bradycardia has been responsive to atropine intravenous administration**.**

Blurred vision, diaphoresis, headache, and impaired psychomotor skills may be observed. Myoclonus and tonic-clonic seizures have been reported. An increasing depth of coma has been observed at higher doses.

There are reports of compromise in the rate and depth of respiration and of life-threatening respiratory depression, necessitating intubation and ventilation. Cheyne-Stokes respiration and apnoea have been observed.

Hypernatremia with metabolic alkalosis has been reported.

Document ratification details

Ratification Process	**Details**
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ACTION: Please add medication to Patient Medical Record

Date: GP Practice:

Dear Dr

Name: **DOB:** **NHS No:**

Address:

Diagnosis:

Medication:

This letter is to inform you that the above patient is receiving medication which is supplied and clinically managed by Royal Papworth Hospital. Please manually record the above medicines on the patient's record on your GP prescribing system to ensure the patient's medication list is complete. Details of how to do this are included on the following pages.

Should you have any questions or concerns please contact the Pharmacy Homecare Team at Royal Papworth Hospital.

Yours sincerely,

Richard Chapple
Principal Pharmacy Technician Homecare Services

How to record Hospital Prescribed Medicines on GP Prescribing Systems

It is important to record all medicines prescribed by the hospital (for which the hospital retain prescribing responsibility) on the GP prescribing system individual patient record.

Potential risks of not recording hospital prescribed medicines include:

- Inadvertent co-prescribing of interacting medicines.
- the potential to miss side effects or not attribute them to drug therapy.
- hospital prescribed medicines will not be recorded on the Summary Care Record.
- potential for doses to be missed if a person is admitted to a different hospital provider It is not necessary or practical to record accurate details of the formulation and dose if the hospital has accepted ongoing prescribing responsibility, because details may change frequently.
  - ➔ Select the nearest match strength and formulation from the pull-down menu.
  - ➔ Select the free-text dose option and enter "dose and formulation managed by Royal Papworth Hospital".

It is equally important to remove the details when the hospital informs the practice that the medicine has been stopped.

EMIS

1. Retrieve the patient record.
2. Follow the usual method of adding a medication to a patient's record but under **dosage** add text to indicate who issues the medication:

   For Hospital medication add "HOSPITAL ONLY, issued by Royal Papworth Hospital".
3. For **quantity** enter 1 as EMIS will not accept no number or 0.
4. If required deal with any safety alerts or other message which are shown.
5. Select **Issue.**
6. On Issue window, expand the **Change All** tab at the top of the screen and select:
   Hospital (No Print) for hospital medications
7. Click **Approve and Complete** to finish.

Vision InPS

Refer to the online training guide "Consultation Manager – Therapy":
Record medicines in the Therapy Add using the picklist under **Source of Drug:**

- Drugs prescribed by a hospital doctor or consultant.

TPP SystmONE

- Right click on the Medication node of the Clinical Tree;
- Select **Record Other Medication;**
- Enter the name of the medication you are recording in the **Drug and Appliance** window;
- Click **Search;**
- Select the particular formulation of the drug you require;
- Click **OK;**
- Choose a **Medication Source**;
- Enter any information about the dose and quantity that you have;
- Click **OK.**

Once **saved** any medications added following the above will appear in the patient's Summary Care Record.

Cambridgeshire & Peterborough Integrated Care System

NHS Cambridgeshire & Peterborough

Appendix 2: Prescription Receipt Confirmation Slip

NHS Royal Papworth Hospital NHS Foundation Trust

Royal Papworth Hospital NHS Foundation Trust

Sodium Oxybate Prescription Checklist

Trust:	Royal Papworth Hospital NHS Foundation Trust	**Date Posted:**
Completed By:		
Direct Telephone:	01223 638540	
E-mail:	phn-tr.pharmacyhomecare@nhs.net	

List ID Number:

Patient ID	NHS Number	Notes	Received

Please can you confirm receipt by Signing below and emailing this form back to: phn-tr.pharmacyhomecare@nhs.net

Name:
Date received:

Compassion Excellence Collaboration

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