Regional Medicines Optimisation Committee (RMOC) Advisory Statement

Sodium Oxybate
Commissioning in adult patients with narcolepsy with cataplexy
Clinical decision criteria

October 2019

Advisory statement

The Regional Medicines Optimisation Committee (RMOC) (Midlands and East) reviewed issues pertaining to the prescribing and commissioning of sodium oxybate in adult patients (≥19 years) with narcolepsy with cataplexy. This topic was initially raised through the RMOC system due to inconsistencies across England regarding access to sodium oxybate when a patient prescribed sodium oxybate as a child transitions to adulthood.

NHS England currently commission sodium oxybate for post-pubescent children weighing ≥40kg and up to their 19th birthday if they meet the strict criteria within the policy. Once the patient passes their 19th birthday, commissioning responsibility transfers to local CCGs, which has led to variation across England. Sodium oxybate is not included within the National tariff payment system.

This document aims to facilitate local decisions by a CCG on whether to commission sodium oxybate for use in adult patients. It suggests a framework by which a CCG can ensure that sodium oxybate is used appropriately and safely under the strict criteria set out in this statement. This statement does not stipulate that sodium oxybate must be commissioned, but aims to assist this decision making process and improve consistency.

The RMOC concluded that this document could be used to facilitate commissioning decisions relating to sodium oxybate for all adult patients, not just patients transitioning to adult services after treatment under NHS England paediatric policy.

NHS England Specialised Commissioning, together with NHS Improvement, will develop a framework for adult services clinicians to consider when children on sodium oxybate transition to adult services. In the interim, adult patients with narcolepsy with cataplexy who have transitioned from paediatric care should continue to receive sodium oxybate, providing there is a demonstrable ongoing clinical need; continuity of care should not be compromised.

Adult patients currently receiving sodium oxybate should also be reviewed to ensure that the treatment remains effective and that there is an ongoing need.

Appendix 1 provides a summary of patient cohort, commissioner, and relevant guidance/policy documents.

Criteria for Commissioning of sodium oxybate in adult patients

The following criteria have been drawn up in consultation with specialist sleep clinicians and NHS England Specialised Commissioning. They are offered as the basis for local commissioning decisions for adult patients.

- Patients presenting with narcolepsy with cataplexy according to International Classification of sleep disorders 3 (ICSD) criteria for Narcolepsy Type 1 AND
- Patients ≥ 19 years old AND
- Where patients have co-morbidities, which are also affecting sleep, these should be managed and adequately treated (for example moderate to severe obstructive sleep apnoea or restless legs syndrome) AND
- Failure to respond to non-pharmacological treatments consisting of behavioural and environmental adaptations, for example planned naps AND
- Inadequate response (within 3 months) to, or intolerable adverse effects from, or contra-indicated use of, more than one stimulant for narcolepsy, *and* more than one anticataplectic agent AND
- Assessed as being able to benefit from sodium oxybate via a specialist sleep centre.

Sodium oxybate is generally considered as a final treatment option for patients. Therefore, consideration needs to be given to the consequences of not allowing a patient access to sodium oxybate, how the patient will be managed in the future, and the impact this might have on the patient's quality of life.

The patient should be fully consulted at all stages of the process and should be fully involved in the decision on appropriate treatment options.

Assessing need for ongoing treatment

- Patients who show signs of serious adverse events should discontinue therapy.
- Improvements in narcolepsy and/ or cataplexy should be determined by expert clinical review, which will include the use of the Epworth Sleepiness Scale and an assessment of symptomatic/quality of life improvements.
- Discontinue if there is inadequate response at 3 months for both cataplexy and narcolepsy. Measurements should ideally be compared to scores prior to sodium oxybate treatment (see **Appendix 2** for definitions). Expert clinical review and patient history will also contribute to this assessment.
- Patients on established therapy should be reviewed at least annually if stable (more frequently if not) to ensure continued benefit.
- Trial withdrawal periods can be considered if this is clinically appropriate.

Background

Narcolepsy is a rare chronic neurological condition affecting the brain's ability to regulate normal sleep/wake cycles, leading to symptoms such as excessive daytime sleepiness, uncontrollable sleep attacks, episodes of conscious collapse (cataplexy—see below), hypnogogic hallucinations (vivid dream-like episodes of seeing, hearing and feeling just before sleep), disturbed night-time sleep (including dream enactment), and sleep paralysis. The estimated prevalence is 40 per 100,000 UK population. It can be extremely debilitating.

About 70% of patients with narcolepsy also have cataplexy which presents as a transient bilateral attack of muscle weakness due to sudden loss of muscle tone, typically lasting less than 2 minutes. Episodes are often precipitated by strong emotional responses, such as laughter, surprise, fear, or anger. Consciousness is retained unless an episode evolves into sleep. Approximately 30% of cases are severe enough to warrant anticataplectic treatment.

Sodium oxybate is licensed for the treatment of narcolepsy with cataplexy in adult patients. There is no currently accepted guidance on the treatment of narcolepsy (with or without cataplexy) in the UK for adult patients. Treatment therefore relies upon specialist knowledge, locally accepted practice, and non-UK guidance. Sodium oxybate is usually considered when all other treatment options have failed.

Current commissioning arrangements

The NHS England commissioning policy allows the use of sodium oxybate for post-pubescent children (weighing >40kg and up to their 19th birthday) where attempts to control symptoms of narcolepsy with cataplexy have failed despite a trial of first and second line medications from each symptom group for at least three months. Governance and monitoring arrangements are clearly laid out within the policy.

Clinical evidence for adult patients

The committee noted the published evidence for sodium oxybate, a summary of which is below.

A systematic review and meta-analysis published in 2012, looked at published and unpublished randomised controlled trial (RCT) data, up until October 2010. Six RCTs were identified: 5 compared against placebo, and one included a comparison of modafanil versus sodium oxybate. Total number of patients from all the trials was 741, and the duration ranged from 2–12 weeks.

All of the efficacy outcomes reported for reduced cataplexy and daytime sleepiness, favoured sodium oxybate compared to placebo, and were statistically significant. The exception was increasing REM sleep versus placebo, which did not reach statistical significance. Improvements were generally dose related.

Limitations to the studies identified included small sample sizes, wide confidence intervals in several cases, and short follow-up periods. Most of the trials were industry funded.

From the 2012 meta-analysis, nausea, vomiting and dizziness were statistically significantly higher with sodium oxybate compared to placebo. In one open-label study, 56% adults reported an adverse event of which 2% were considered serious. Study withdrawals due to adverse events were reported and were all less than 10% of participants.

Trials published since the 2012 systematic review showed broadly similar outcomes. The clinical response appears to be dose-related.

Cost-analysis

No studies were identified assessing the cost-effectiveness of sodium oxybate for narcolepsy with cataplexy in either adult or paediatric patients. Due to the small numbers of patients enrolled in trials, a robust assessment of cost-effectiveness is not possible at this time.

The cost of sodium oxybate varies with the dose, which ranges from 4.5 g to 9g daily. This results in an estimated cost per patient of £6,570 to £13,140 per year (July 2019). Mean doses used in practice are likely to be in the middle of that range.

In December 2016, NHS England estimated that there are around 10 paediatric patients newly diagnosed per year. At the time there were 10 children treated with sodium oxybate nationally.

Patient access

Sodium oxybate should be initiated and titrated to effect in secondary or tertiary care by a specialist sleep centre with expertise in treating narcolepsy, including experience in use of sodium oxybate.

Ongoing prescribing responsibility should be determined locally, however the monitoring and review of these patients should be continued by the specialist sleep centre. It should be noted that sodium oxybate is a controlled drug (Schedule 2).

The specialist sleep centre must have access to a sleep laboratory that can conduct standard polysomnography and multiple sleep latency tests to AASM standards. The specialist sleep centre should involve a multi-disciplinary team, including consultants and access to a range of other specialities which may include psychology, psychiatry, specialist pharmacists, and sleep technologists.

Limitations

This statement does not consider the suitability for the use of sodium oxybate outside of its licensed indication, since this is beyond its scope.

This statement does not directly consider the place in therapy of pitolisant. However, it is acknowledged that pitolisant is also licensed for this indication.

Consultation

The production of this position statement involved consultation with RMOC members, plus the following:

- Dr Manny Bagary, Consultant Somnologist and Neuropsychiatrist, Birmingham and Solihull Mental Health NHS Foundation Trust
- Dr Andrew Hall, Consultant in Anaesthesia, Intensive Care & Sleep Disorders Medicine, University Hospitals of Leicester NHS Trust
- Dr Timothy Quinnell, Consultant Respiratory Physician, Royal Papworth Hospital NHS Foundation Trust
- Elaine Lyons, Highly specialised pharmacist—Sleep and Respiratory Medicine, Guy's and St Thomas' NHS Foundation Trust
- Specialised Commissioning, NHS England
- British Sleep Society—endorsement.

Declaration of Interest Statement

Dr Manny Bagary and Elaine Lyons have not declared any conflicts of interest.
The British Sleep Society is a UK-registered charity that aims to improve public health by promoting education and research into sleep and its disorders and treatment. The British Sleep Society receives sponsorship for its annual conference from UCB Pharma in line with responsible UK pharmaceutical sponsorship requirements.
Dr Andrew Hall has previously received travel and expenses from a number of pharmaceutical companies, including UCB Pharma, for past educational meetings; he is a member of the British Sleep Society. Dr Timothy Quinnell has previously received travel, accommodation and conference registration from UCB Pharma for past conferences. Timothy Quinnell is president of the British Sleep Society.

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Appendix 1

Table 1: Patient cohort, commissioning responsibility, and relevant policy/guidance

Patient Cohort	Commissioner	Policy/Guidance
Child <19 years (>40kg)	NHS England	NHS England Clinical Commissioning Policy: Sodium oxybate for symptom control of narcolepsy with cataplexy (children)
Adult ≥ 19 years (transitioning from paediatric care)	CCG	RMOC Advisory Statement (interim position until NHS England/NHS Improvement transitioning framework published)
Adults ≥ 19 years (sodium oxybate treatment naïve)	CCG	RMOC Advisory Statement
Adults ≥ 19 years currently receiving sodium oxybate treatment	CCG	Review appropriateness of continued treatment as per RMOC Advisory Statement

Appendix 2

Measuring Response to sodium oxybate treatment

Cataplexy
At least one cataplexy score (either severity or frequency) should improve after 3 months of therapy. Measurements should be compared to scores prior to sodium oxybate treatment.

Severity of cataplexy
- 1 = moderate weakness
- 2 = can maintain posture with external support
- 3 = loses posture and falls to the ground

Frequency of cataplexy
- 0 = < 1 episode per year
- 1 = ≥ 1 attack per year
- 2 = more than one attack per month
- 3 = > 1 attack per week
- 4 = > 1 per day

Narcolepsy
Improvements in narcolepsy should be determined by expert clinical review, which will include the use of the Epworth Sleepiness Scale and an assessment of symptomatic/quality of life improvements.

Document control

Document location
Copies of this document can be obtained from https://www.sps.nhs.uk/

Revision History

Revision Date	Actioned by	Summary of changes	Version

Approvals

Name	Date of Approval	Version
RMOC Midlands and East	08.08.2019	1.3 Draft
RMOC (national)	08.07.2019	Draft
NHS England	09.09.2019	1.3 Draft

Further information

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If you have a Medicines Optimisation issue which is affecting current practice raise a topic

Disclaimer

This statement represents the views of the RMOC system, arrived at after consideration of the best available evidence. The committees include a range of stakeholder representatives who have helped shape the advice. Membership of the committee can be viewed via the **SPS website.** This advice is not mandatory, but commissioners and providers are expected to take this statement into account, alongside the individual needs, preferences and values of patients and service users. The statement does not override the responsibility to make decisions appropriate to the circumstances of the individual. However, commissioners and providers have a responsibility to consider implementing this statement, in their local context, in the light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this statement should be interpreted in a way which would be inconsistent with compliance with those duties.