IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Sodium oxybate (Xyrem®) is a medication used to reduce the number of cataplexy (weak or paralyzed muscles) attacks and to reduce excessive daytime sleepiness in patients with narcolepsy. Sodium oxybate is a schedule III controlled substance.
Policy/Criteria

I. Most contracts require prior authorization approval of sodium oxybate prior to coverage. Sodium oxybate may be considered medically necessary for members with the following diagnoses when criterion A or B below is met.

A. Cataplexy (a sudden loss in muscle tone and deep tendon reflexes) associated with narcolepsy.

OR

B. Excessive daytime sleepiness associated with narcolepsy when:

1. Modafinil in doses up to 400 mg daily, or armodafinil in doses up to 250 mg daily, has been ineffective, not tolerated, or contraindicated.

AND

2. At least one other formulary/preferred treatment, such as methylphenidate or dextroamphetamine, has been ineffective, not tolerated, or contraindicated.

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers sodium oxybate to be a self-administered medication.

B. When prior authorization is approved, sodium oxybate may be covered in quantities up to 9 grams per night.

C. Authorization shall be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Sodium oxybate is considered not medically necessary for the following condition(s):

A. Fibromyalgia.

IV. Sodium oxybate is considered investigational for other conditions or applications, including, but not limited to, the treatment of:

A. Alcohol dependence and withdrawal.

B. Myoclonus and essential tremor

C. Night eating syndrome.

D. Opioid dependence and withdrawal.

E. Parkinsonism.

F. Primary obstructive sleep apnea
Position Statement

Clinical Efficacy

CATAPLEXY/ NARCOLEPSY

- There is no useful evidence that sodium oxybate is more effective than oral stimulants, such as methylphenidate, dexamphetamine, modafinil, or armodafinil, in relieving the symptoms of cataplexy associated with narcolepsy or excessive daytime sleepiness associated with narcolepsy.

* In trials with uncertain usefulness, sodium oxybate showed statistically significant reduction in the weekly cataplexy attacks compared to placebo after 4 weeks of treatment, by about 6 to 12 attacks per week, compared to patients receiving placebo. Note that more than 80% of subjects were also taking modafinil during the trial, making it impossible to separate the effect of each medication. [1-5]

* Patients with excessive daytime sleepiness randomized to sodium oxybate showed a statistically significant, but modest improvement, in scores on rating scales to assess sleepiness and maintenance of daytime wakefulness compared to patients taking placebo after 8 weeks of treatment. Note that more than 75% of subjects were also taking modafinil during the trial, making it impossible to separate the effect of each medication. [1, 6, 7]

- There is no useful evidence that combining sodium oxybate with modafinil substantially reduces drowsiness over either agent alone. [1, 6]

- There is no useful evidence to support use of sodium oxybate in the treatment of conditions other than cataplexy in narcolepsy.

- The safety and effectiveness of sodium oxybate doses > 9 grams per night have not been established. [1]

FIBROMYALGIA

- The most recent national fibromyalgia treatment guidelines from the American Pain Society include the following recommendations: [8]

* Non-drug therapies such as exercise and cognitive behavioral therapy are recommended as a foundation of treatment.

* Tricyclic antidepressants (TCAs) (e.g., amitriptyline, desipramine) or cyclobenzaprine are considered first-line medication options, and provide the best value for patients.

* Serotonin reuptake inhibitors (e.g., fluoxetine) or tramadol (with or without acetaminophen) may also be used with or without TCAs or cyclobenzaprine.

- Sodium oxybate is not currently recognized as a treatment option for fibromyalgia in the current national guidelines. [8]
Four published clinical trials have evaluated the efficacy of sodium oxybate in the management of patients with fibromyalgia. [9-12] Although suggestive of efficacy, these trials have significant flaws, including high rates of subject non-completion, which makes the results of these trials uncertain.

There is no evidence sodium oxybate is safer or more effective than standard treatments for fibromyalgia.

**Investigational Uses**

**ALCOHOL DEPENDENCE AND WITHDRAWAL**

- The evidence for the sodium oxybate in alcohol dependence and withdrawal is limited to one small trial in outpatients, along with other very small trials generally administered as part of an inpatient admission.

- All four small randomized controlled trials have reported reduction of symptoms related to alcohol withdrawal compared to placebo, clomethiazole, diazepam, or oxazepam, [13-15, 28]. These trials examined the use of sodium oxybate on alcohol craving, alcohol consumption and/or abstinence. While suggestive of a useful effect, more studies are needed to fully understand the role of sodium oxybate for the management of alcohol abuse.

**OBSTRUCTIVE SLEEP APNEA**

- Small, exploratory studies have been conducted to evaluate the safety of sodium oxybate in patients with obstructive sleep apnea. [19]. Although suggestive, larger, better designed randomized controlled trials are needed to evaluate whether the benefits of sodium oxybate outweigh the risks in this patient population.

**OTHER**

- Sodium oxybate has been studied in small, preliminary trials for possible efficacy in opiate withdrawal syndrome, parkinsonism, essential tremor, and night-eating syndrome. Further research is needed to establish the clinical safety and efficacy of sodium oxybate for these indications. [20-25]

**Safety**

- Contraindications to the use of sodium oxybate include: [1]
  - Concomitant treatment with sedative hypnotic agents.
  - Use in patients with succinic semialdehyde dehydrogenase deficiency. This rare disorder is an inborn error of metabolism variably characterized by mental retardation, hypotonia, and ataxia.

- **Boxed Warning** [1]
  - Sodium oxybate should not be used with alcohol or other central nervous system (CNS) depressants. It is the same chemical as gamma hydroxybutyrate (GHB), a known drug of abuse. Abuse has been associated with some important CNS adverse events (including death). Even at recommended doses, use has been
associated with confusion, depression and other neuropsychiatric events. Reports of respiratory depression occurred in clinical trials. Almost all of the patients who received sodium oxybate during clinical trials were receiving CNS stimulants.

* Important CNS adverse events associated with abuse of GHB include seizure, respiratory depression and profound decreases in level of consciousness, with instances of coma and death. For events that occurred outside of clinical trials, in people taking GHB for recreational purposes, the circumstances surrounding the events are often unclear (e.g., dose of GHB taken, the nature and amount of alcohol or any concomitant drugs).

* Sodium oxybate is available through the Xyrem Success Program, using a centralized pharmacy 1-866-XYREM88® (1-866-997-3688). The Success Program provides educational materials to the prescriber and the patient explaining the risks and proper use of sodium oxybate, and the required prescription form. Once it is documented that the patient has read and/or understood the materials, the drug will be shipped to the patient. The Xyrem Success Program also recommends patient follow-up every 3 months. Physicians are expected to report all serious adverse events to the manufacturer.

Deaths [26, 27]

Deaths have been reported in the literature associated with the therapeutic use of sodium oxybate. These cases varied in diagnosis and individual circumstance, but underscore the importance of using sodium oxybate only in clinical situations where there is reliable clinical evidence that the benefit of treatment outweighs the risk.

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References

7. Weaver TE, Cuellar N. A randomized trial evaluating the effectiveness of sodium oxybate therapy on quality of life in narcolepsy. Sleep. 2006 Sep 1;29(9):1189-94.

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