Xyrem® (sodium oxybate) Prior Authorization Criteria

FDA APPROVED INDICATIONS AND DOSAGE

**FDA Indication:** Treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy.  

**Dosing:** Recommended starting dose is 4.5 g/night divided into two equal doses of 2.25 g. First dose should be taken at bedtime, while sitting up in bed, and the second should be taken again 2.5-4 hours later. Effective dose is 6 to 9 g/night and titration should be done in increments of 1.5 g/night (0.75 g/dose) with 1-2 weeks between dose increases. Doses greater than 9 g/night are not recommended. Dilute each dose with 2 oz. of water. Sodium oxybate is available as 500 mg/ml oral solution.

**CLINICAL RATIONALE**

**Efficacy**

Xyrem (sodium oxybate) is the only drug currently approved for the treatment of cataplexy in patients with narcolepsy. Antidepressants such as fluoxetine, amitriptyline, and duloxetine are also used off-label for this indication, but there is a lack of evidence to support their use. The efficacy of sodium oxybate has been established in three double-blind, placebo controlled trials. Doses ranging from 4.5 to 9 g/night were shown to significantly reduce the number of weekly cataplexy attacks by 57-84%, depending on the dose. This is significant in comparison to a 21-28% reduction seen in the placebo groups. In clinical trials, approximately 80% of patients were using a stimulant concomitantly with sodium oxybate, making it difficult to determine the efficacy of sodium oxybate alone. Even though sodium oxybate has had positive results in clinical trials, its current place in the treatment of cataplexy is undetermined. The European Federation of Neurological Societies (EFNS) recommends sodium oxybate as a first line treatment for cataplexy. In contrast, the Scottish Medicines Consortium does not recommend the use of sodium oxybate at all. Several review articles conclude that sodium oxybate should be used as an alternative to antidepressants. Concerns with first line use include abuse potential, lack of data regarding monotherapy, difficult dosing, high cost, and risk of respiratory depression.

The EFNS recognizes sodium oxybate as a potential first-line therapy for excessive daytime sleepiness and this is in concordance with review articles evaluating its place in therapy. Data indicates that stimulants such as modafinil are the initial drugs of choice. However, the use of sodium oxybate as a first line treatment for excessive daytime sleepiness is increasing. Although sodium oxybate is deemed efficacious, more comparative studies are needed to determine which medication is the optimal first-line treatment for this indication.
Safety
There are disadvantages associated with the use of sodium oxybate, including its safety concerns and potential for abuse. As the sodium salt of gamma hydroxybutyrate (GHB), it has been used illegally as a date-rape drug. Sodium oxybate is a schedule III substance which holds a black box warning indicating a risk of neuropsychiatric events and respiratory depression, and discourages use with alcohol or other central nervous system depressants. Sodium oxybate is contraindicated in patients currently taking sedative hypnotic agents and in patients with succinic semialdehyde dehydrogenase deficiency. The Xyrem Success Program restricts distribution to one pharmacy and requires physicians to register to prescribe.

Off-Label Use - Fibromyalgia
Sodium oxybate is currently undergoing Phase III clinical trials for the treatment of fibromyalgia. Doses ranging from 4.5g/night to 6 g/night significantly reduced both pain and sleep disturbances in patients with fibromyalgia. A 2008 review reported one randomized double-blind placebo-controlled study of 24 patients in which sodium oxybate 6.0 g/night was effective in reducing sleep abnormalities, pain and fatigue associated with fibromyalgia. It significantly improved 3 of 4 pain scores and 3 fatigue scores compared with placebo; it significantly decreased sleep latency, alpha intrusion, and REM sleep compared to placebo; and it increased stage 3-4 sleep compared with placebo. The authors of the review ranked sodium oxybate as having moderate evidence of efficacy in fibromyalgia but with the evidence supporting its efficacy as less compelling than that of other drugs (e.g. tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, pregabalin or gabapentin). The manufacturer has recently submitted an application to the FDA for expanded labeling of the drug upon receiving positive results in clinical trials.

For additional clinical information see Prime Therapeutics Formulary Chapter 9.6G: Anti-Catataplectic Agents

REFERENCES
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OBJECTIVE
The intent of the Xyrem Prior Authorization (PA) Criteria is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies and according to dosing recommended in product labeling. The PA criteria will approve Xyrem when prescribed according to product labeling for patients 16 years and older. Safety and effectiveness in individuals below 16 years of age have not been established. The PA criteria will consider Xyrem to be a first-line agent for treatment of cataplexy and a second-line agent to a stimulant for patients with a diagnosis of narcolepsy with excessive daytime sleepiness. Xyrem will not be covered for patients with a listed contraindication: patient is using a sedative hypnotic agent concurrently or patient has succinic semialdehyde dehydrogenase deficiency. Patients receiving Xyrem must be enrolled in the Xyrem Success Program.

TARGET DRUGS
Xyrem (sodium oxybate)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Xyrem will be approved when ALL of the following are met:

1. The patient is 16 years of age or older AND
2. ONE of the following:
   a. The patient has a diagnosis of narcolepsy with cataplexy OR
   b. The patient has a diagnosis of narcolepsy with excessive daytime sleepiness AND has tried and failed or has an allergy, intolerance, or contraindication to a standard stimulant agent AND
3. The prescriber has documented that the patient is enrolled in the Xyrem Success Program AND
4. The patient does not have succinic semialdehyde dehydrogenase deficiency AND
5. The patient is not being treated with a sedative hypnotic agent AND
6. The requested dose is at or below the FDA-labeled maximum dose of 9 gm/night (540 mL/30 days)

Length of Approval: 12 months
**Xyrem® (sodium oxybate) Prior Authorization**

**ELECTRONIC EDIT**
The overall process for a prior authorization will not allow the targeted drugs to adjudicate through the claims system. When a patient requests a targeted drug the system will reject the claim with the message indicating that prior authorization is necessary.

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
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<tbody>
<tr>
<td>Xyrem (sodium oxybate)</td>
<td>62450060******</td>
<td>M, N, O, or Y</td>
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<tr>
<td>500 mg/mL oral solution (180 mL bottle)</td>
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**PRIOR AUTHORIZATION CRITERIA QUESTION SET**

**Initial and Renewal Evaluation**

1. Is the patient 16 years of age or older?
   If yes, continue to 2. If no, deny.

2. Does the patient have a diagnosis of narcolepsy with cataplexy?
   If yes, continue to 6. If no, continue to 3.

3. Does the patient have a diagnosis of narcolepsy with excessive daytime sleepiness?
   If yes, continue to 4. If no, deny.

4. Is the patient currently receiving or has the patient previously tried and failed therapy with a standard stimulant agent (modafinil, armodafinil, methylphenidate, dextroamphetamine, or amphetamine/dextroamphetamine)?
   If yes, continue to 6. If no, continue to 5.

5. Does the patient have an allergy, contraindication, or intolerance to standard stimulant treatment?
   If yes, continue to 6. If no, deny.

6. Has the prescriber documented that the patient is enrolled in the Xyrem Success Program?
   If yes, continue to 7. If no, deny.

7. Does the patient have succinic semialdehyde dehydrogenase deficiency?
   If yes, deny. If no, continue to 8.

8. Is the patient being treated with any sedative hypnotic agents?
   If yes, deny. If no, continue to 9.

9. Is the requested dose at or below the FDA-labeled maximum dose of 9 gm/night (540 mL/30 days)?
   If yes, approve for 12 months. If no, deny.