VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Neurology – Oxybate Products Prior Authorization Policy
- Lumryz™ (sodium oxybate extended-release oral suspension – Avadel)
- Xyrem® (sodium oxybate oral solution – Jazz, generic)
- Xywav® (calcium, magnesium, potassium, and sodium oxybates oral solution – Jazz)

REVIEW DATE: 06/26/2024; selected revision 11/13/2024

OVERVIEW

Lumryz, sodium oxybate oral solution, and Xywav, central nervous system (CNS) depressants, are indicated for the following uses:[1-3]

- **Cataplexy treatment in patients with narcolepsy**. Lumryz, Sodium oxybate oral solution and Xywav are indicated in patients ≥ 7 years of age.
- **Excessive daytime sleepiness in narcolepsy**. Lumryz, Sodium oxybate oral solution and Xywav are indicated in patients ≥ 7 years of age.

Additionally, Xywav is indicated for the treatment of **idiopathic hypersomnia** in adults.[2]

Two specialized tests, which can be performed in a sleep disorders clinic, are required to establish a diagnosis of narcolepsy or idiopathic hypersomnia.[4] Polysomnography is an overnight recording of brain and muscle activity, breathing, and eye movements. The multiple sleep latency test (MSLT) assesses daytime sleepiness by measuring how quickly a person falls asleep and whether they enter rapid eye movement (REM) sleep. Polysomnography is routinely indicated for the diagnosis of sleep-related breathing disorders; for continuous positive airway pressure titration in patients with sleep-related breathing disorders; with an MSLT in the evaluation of suspected narcolepsy; and in certain atypical or unusual parasomnias.[5] The MSLT is indicated as part of the evaluation of patients with suspected narcolepsy to confirm the diagnosis or patients who are thought to have idiopathic hypersomnia to exclude other causes of hypersomnia. Most patients with narcolepsy have objective evidence of hypersomnia as determined by a mean sleep latency < 5 minutes. In studies, the presence of two or more sleep-onset REM episodes (SOREMPs) was associated with a sensitivity of 0.78 and a specificity of 0.93 for the diagnosis of narcolepsy. SOREMPs do not occur exclusively in patients with narcolepsy; thus, it is important to rule out or treat other sleep disorders before evaluating SOREMPs in the diagnosis of narcolepsy. Diagnostic criteria for patients with idiopathic hypersomnia include a mean sleep latency ≤ 8 minutes and MSLT results showing < 2 SOREMPs or no SOREMPs if the REM sleep latency preceding polysomnogram is ≤ 15 minutes; also, these patients do not have cataplexy. For these reasons, polysomnography and an MSLT performed on the day after the polysomnographic evaluation are routinely indicated in the evaluation of suspected narcolepsy or idiopathic hypersomnia.

Guidelines

Pertinent medical guidelines related to oxybate products are summarized below; of note, Lumryz and Xywav are not addressed in any of the guidelines.

Narcolepsy and Cataplexy

The American Academy of Sleep Medicine (AASM) practice parameters for the treatment of central disorders of hypersomnolence were updated in 2021.[6,7]

- Modafinil, Wakix® (pitolisant tablets), sodium oxybate, and Sunosi® (solriamfetol tablets) are recommended as effective treatments for daytime sleepiness due to narcolepsy and reducing disease severity in adults (Strong Recommendation for each).
- Wakix and sodium oxybate have also demonstrated efficacy for the treatment of cataplexy in patients with narcolepsy (Strong Recommendation for each).
- Sodium oxybate and armodafinil have Conditional Recommendations for the treatment of narcolepsy, showing efficacy for daytime sleepiness due to narcolepsy and reducing disease severity.
- Dextroamphetamine has a Conditional Recommendation for the treatment of narcolepsy, showing efficacy for excessive daytime sleepiness and cataplexy.
- Methylphenidate has a Conditional Recommendation for the treatment of narcolepsy, showing efficacy in reducing disease severity.
- There was insufficient and inconclusive evidence to make recommendations for l-carnitine, scheduled naps, selegiline, triazolam, selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs).
- Modafinil and sodium oxybate have Conditional Recommendations for the treatment of narcolepsy in pediatric patients.

Note: A Strong Recommendation should be followed by clinicians under most circumstances. A Conditional Recommendation requires that the clinician use clinical knowledge and experience and strongly consider the individual patient's values and preferences to determine the best course of action.

Idiopathic Hypersomnia

The AASM guideline includes recommendations for the treatment of idiopathic hypersomnia.[6,7]

- Only modafinil has a Strong recommendation for use.
- Clarithromycin, methylphenidate, Wakix, and sodium oxybate have Conditional recommendations for the treatment of idiopathic hypersomnia in adults.

Safety

Sodium oxybate is the sodium salt of gamma hydroxybutyrate (GHB) and Xywav is a mixed salt formulation of GHB.[1-3] They are both Schedule III controlled substances. Abuse of GHB (a Schedule I controlled substance), either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death. Because of the risks of CNS depression, abuse, and misuse, sodium oxybate oral solution and Xywav are available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS) called the Xyrem/Xywav Success Program, using a centralized pharmacy. Healthcare professionals who prescribe sodium oxybate oral solution or Xywav and patients must enroll in the Xyrem/Xywav Success Program and must comply with the requirements to ensure the drug's safe use. Similarly, Lumryz is only available through a restricted distribution program under a REMS called the Lumryz REMS. Healthcare providers who prescribe Lumryz must be specially certified; Lumryz will be dispensed only by pharmacies that are specially certified; and Lumryz will be dispensed and shipped only to patients who are enrolled in the Lumryz REMS with documentation of safe use conditions.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Lumryz, sodium oxybate oral solution, and Xywav. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Lumryz, sodium oxybate oral solution, and Xywav as well as the monitoring required for adverse event and long-term efficacy, approval requires these products to be prescribed by a physician who specializes in the condition being treated.

Automation: Continuation of Therapy is not clinically necessary for the Oxybate Products. Refer to the AUM reference guide for additional information.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Lumryz, sodium oxybate oral solution, or Xywav is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Cataplexy Treatment in a Patient with Narcolepsy.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 7 years of age; AND
   - **B)** Patient has been evaluated using polysomnography and a multiple sleep latency test; AND
   - **C)** Diagnosis of narcolepsy has been confirmed, according to the prescriber; AND
   - **D)** The medication has been prescribed by a sleep specialist physician or a neurologist; AND
   - **E)** Patient meets ONE of the following (i or ii);
     - **i.** Patient has tried dextroamphetamine; OR
     - **ii.** Patient has a contraindication or intolerance to dextroamphetamine, according to the prescriber.
       Note: Contraindications to dextroamphetamine include a history of substance use disorder; advanced arteriosclerosis, symptomatic cardiovascular disease, and/or moderate to severe hypertension; hyperthyroidism; known hypersensitivity to sympathomimetic amines; glaucoma; agitated states; and concomitant administration with monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOIs.

2. **Excessive Daytime Sleepiness in a Patient with Narcolepsy.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 7 years of age; AND
   - **B)** Patient has been evaluated using polysomnography and a multiple sleep latency test; AND
   - **C)** Diagnosis of narcolepsy has been confirmed, according to the prescriber; AND
   - **D)** The medication has been prescribed by a sleep specialist physician or a neurologist; AND
   - **E)** Patient has tried at least one of the following treatments: a central nervous system (CNS) stimulant, modafinil, or armodafinil.
     Note: Examples of CNS stimulants include methylphenidate, dexmethylphenidate, and dextroamphetamine.

3. **Idiopathic Hypersomnia.** Approve Xywav (NOT sodium oxybate oral solution or Lumryz) for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has been evaluated using polysomnography and a multiple sleep latency test; AND
   - **C)** Results of the polysomnography and a multiple sleep latency test are congruent with a diagnosis of idiopathic hypersomnia, according to the prescriber; AND
   - **D)** The medication has been prescribed by a sleep specialist physician or a neurologist; AND
   - **E)** Patient has tried at least one of modafinil, armodafinil, or methylphenidate.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Lumryz, sodium oxybate oral solution or Xywav is not recommended in the following situations:

1. **Fibromyalgia.** The European League Against Rheumatism (EULAR) issued evidence-based recommendations for the management of fibromyalgia (2016) stating that initial management should involve patient education and focus on non-pharmacological therapies.[8] EULAR's position on sodium oxybate for fibromyalgia is strongly against with 94% agreement. Duloxetine, pregabalin capsules and oral solution, and Savella® (milnacipran tablets) are indicated for the treatment of fibromyalgia.[9-11] Other recommended treatments include tricyclic antidepressants (i.e., amitriptyline), cyclobenzaprine, gabapentin, and selective serotonin reuptake inhibitors (i.e., fluoxetine, sertraline, paroxetine).[12]

2. **Concomitant use of Lumryz, sodium oxybate oral solution, and/or Xywav with each other or an oxybate product used in combination with Wakix (pitolisant tablets) and/or Sunosi (solriamfetol tablets).** Lumryz, sodium oxybate oral solution. and Xywav have the same active ingredient (oxybate, a CNS depressant) and have not been studied for use in combination or as alternating treatments.[1-3] Sunosi, a dopamine and norepinephrine reuptake inhibitor, is indicated to improve wakefulness in adults with excessive daytime sleepiness due to narcolepsy or obstructive sleep apnea.[13] Wakix, an antagonist/inverse agonist of the histamine-3 receptor, is indicated for excessive daytime sleepiness and cataplexy in adults with narcolepsy.[14] Currently, there are no published studies evaluating combination use of these medications.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Xyrem® oral solution [prescribing information]. Palo Alto, CA: Jazz; April 2023.
2. Xywav® oral solution [prescribing information]. Palo Alto, CA: Jazz; April 2023.
3. Lumryz™ extended-release oral suspension [prescribing information]. Chesterfield, MO: Avadel; October 2024.
4. National Institutes of Health. Narcolepsy. National Institute of Neurological Disorders and Stroke. Last reviewed November 28, 2023. Available at: https://www.ninds.nih.gov/health-information/disorders/narcolepsy?search-term=narcolepsy. Accessed on June 24, 2024.
5. Krahn LE, Arand DL, Avidan AY, et al. Recommended protocols for the multiple sleep latency test and maintenance of wakefulness test in adults: guidance from the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2021;17(12):2489-2498.
6. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. Available at: https://jcsm.aasm.org/doi/10.5664/jcsm.9328. Accessed on June 24, 2024.
7. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med*. 2021;17(9).
8. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis*. 2017;76(2):318-328.
9. Lyrica® capsules and oral solution [prescribing information]. Morgantown, WV: Viatris; December 2023.
10. Cymbalta® delayed-release capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
11. Savella® tablets [prescribing information]. North Chicago, IL: AbbVie; May 2024.
12. Clauw DJ. Fibromyalgia: a clinical review. *JAMA*. 2014;311(15):1547-1555.
13. Sunosi® tablets [prescribing information]. New York, NY: Axsome; June 2023.
14. Wakix® tablets [prescribing information]. Plymouth Meeting, PA: Harmony Biosciences; June 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	**Lumryz:** Lumryz was added to the policy. **Cataplexy Treatment in a Patient with Narcolepsy:** The previous age requirement of ≥ 7 years of age was specified to apply to sodium oxybate oral solution and Xywav. An age requirement of ≥ 18 years of age was specified to apply to Lumryz. **Excessive Daytime Sleepiness in a Patient with Narcolepsy:** The previous age requirement of ≥ 7 years of age was specified to apply to sodium oxybate oral solution and Xywav. An age requirement of ≥ 18 years of age was specified to apply to Lumryz. **Conditions Not Recommended for Approval:** Concomitant use of sodium oxybate with Xywav or either oxybate product used in combination with Wakix (pitolisant tablets) and/or Sunosi (solriamfetol tablets) was modified to include Lumryz as a product that should not be used concomitantly with sodium oxybate oral solution, Xywav, Wakix, or Sunosi due to lack of published studies demonstrating additive efficacy.	06/14/2023
Annual Revision	No criteria changes.	06/26/2024
Selected Revision	**Cataplexy Treatment in a Patient with Narcolepsy:** Changed the age requirement for Lumryz from ≥ 18 years of age to ≥ 7 years of age. **Excessive Daytime Sleepiness in a Patient with Narcolepsy:** Changed the age requirement for Lumryz from ≥ 18 years of age to ≥ 7 years of age.	11/13/2024