MEDICAL MUTUAL®

Drug Policy

Policy:	**Narcolepsy Products Prior Authorization Policy**	**Annual Review Date:** **08/22/2024**
Impacted Drugs:	• Wakix (pitolisant tablets – Harmony) • Xyrem (sodium oxybate oral solution – Jazz, generic) • Xywav (calcium, magnesium, potassium, and sodium oxybates oral solution – Jazz) • Lumryz (sodium oxybate extended-release oral suspension – Avadel)	**Last Revised Date:** **01/16/2025**

OVERVIEW

Wakix, an antagonist/inverse agonist of the histamine-3 receptor, is indicated for the following uses:[1]

- **Excessive daytime sleepiness in adults and pediatric patients ≥ 6 years of age with narcolepsy**.
- **Cataplexy in adults with narcolepsy**.

Wakix is the only wakefulness-promoting agent that is not a controlled substance.[1-4]

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 indicated in patients ≥ 7 years of age.**
- **Excessive daytime sleepiness in narcolepsy indicated in patients ≥ 7 years of age.**

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

POLICY STATEMENT

This policy involves the use of Wakix, sodium oxybate oral solution, Lumryz and Xywav. Prior authorization is recommended for pharmacy benefit coverage of Wakix, sodium oxybate oral solution, Lumryz and Xywav. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Wakix, sodium oxybate oral solution, Lumryz and Xywav, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Wakix, sodium oxybate oral solution, Lumryz, and Xywav be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy*.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of **Wakix** is recommended in those who meet the following criteria:

1. Excessive Daytime Sleepiness (EDS) With Narcolepsy

Criteria. *Patient must meet the following criteria (A, B, C, D, and E):*

A) Patient is ≥ 6 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 is prescribed by or in consultation with a sleep specialist physician or a neurologist; AND
E) If the patient is ≥ 18 years of age, then the patient meets ONE of the following (i or ii):
- **i.** Patient has tried generic modafinil or generic armodafinil; OR
  Note: An exception to this requirement is allowed if the patient has previously tried brand Provigil or brand Nuvigil.
- **ii.** Patient has a history of substance use disorder and a wakefulness-promoting agent that is not a controlled substance is necessary, per the prescriber.

2. Cataplexy with Narcolepsy

Criteria. *Patient must meet the following criteria (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) Diagnosis of narcolepsy has been confirmed, according to the prescriber; AND
D) The medication is prescribed by or in consultation with 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; concomitant administration with monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOIs.

Initial Approval/ Extended Approval.
A) *Initial Approval: 1 year*
B) *Extended Approval: 1 year*

Coverage of **Lumryz** is recommended in those who meet the following criteria:

1. Cataplexy Treatment in a Patient with Narcolepsy

Criteria. *Patient must meet the following criteria (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
Criteria. *Patient must meet the following criteria (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.

Initial Approval/ Extended Approval.
A) *Initial Approval: 3 months*
B) *Extended Approval: 1 year*

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

1. Excessive Daytime Sleepiness (EDS) With Narcolepsy
Criteria. *Patient must meet the following criteria (A, B, C, D, and E):*

A. Patient is 7 years or older; AND
B. Patient has tried two of the following treatments: a central nervous system (CNS) stimulant, modafinil or armodafinil; AND
Note: examples of CNS stimulants are methylphenidate, dexmethylphenidate, and dextroamphetamine.
C. If patient is 18 years or older, all of the following (a, b, and c) must be met;
a. Patient has tried Lumryz or has a contraindication to Lumryz; AND
b. Patient has tried Sunosi or has a contraindication to Sunosi or is currently established on the requested product; AND
c. Patient has tried Wakix or has a contraindication to Wakix or is currently established on the requested product; AND
D. Narcolepsy has been confirmed with polysomnography and a multiple sleep latency test (MSLT)*; AND
E. Sodium oxybate/Xywav has been prescribed by a sleep disorder specialist, pulmonologist, psychiatrist, or neurologist.

2. Cataplexy with Narcolepsy

Criteria. *Patient must meet the following criteria (A, B, C, D, and E):*

A. Patient is 7 years of age or older; AND
B. Narcolepsy has been confirmed with polysomnography and a multiple sleep latency test (MSLT)*; AND
C. Sodium oxybate/Xywav has been prescribed by a sleep disorder specialist, pulmonologist, psychiatrist, or neurologist.
D. Patient meets ONE of the following criteria (i or ii);
  a. Patient has tried dextroamphetamine; OR
  b. Patient has a contraindication or intolerance to dextroamphetamine, according to the prescriber; AND

  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.
E. The patient has tried both of the following (a and b):
  a. Wakix or has a contraindication to Wakix or is currently established on the requested product; AND
  b. Lumryz or has a contraindication to Lumryz.

Initial Approval/ Extended Approval.
A) *Initial Approval: 3 months*
B) *Extended Approval: 1 year*

3. Idiopathic Hypersomnia (Xywav only)
Criteria. *Patient must meet the following criteria (A, B, C, D, and E):*

A. Patient is 18 years of age or older; AND
B. The patient has tried at least one of modafinil, armodafinil, or methylphenidate; AND
C. The patient has been evaluated using polysomnography*; AND
D. The patient has been evaluated using MSLT*; AND
E. Must be prescribed by or in consultation with a sleep disorder specialist, pulmonologist, psychiatrist, or neurologist; AND

Initial Approval/ Extended Approval.
A) *Initial Approval: 3 months*
B) *Extended Approval: 1 year*

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Wakix, sodium oxybate oral solution, Lumryz, and Xywav have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Long-Term Maintenance of Fibromyalgia (Xyrem, Lumryz and Xywav).** An FDA advisory panel overwhelmingly rejected the application for approval of Xyrem for the treatment of fibromyalgia on August 20, 2010. This decision was based on conclusions that clinical trials brought forward lacked significant efficacy compared to current fibromyalgia medications on the market. Also, the lack of information detailing drug interactions within the study samples were concerning.

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.

***Documentation Requirements:**

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational, or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

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2. Xywav® oral solution [prescribing information]. Palo Alto, CA: Jazz; April 2023.
3. Lumryz™ extended-release oral suspension [prescribing information]. Chesterfield, MO: Avadel; May 2023.
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.
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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.
15. Provigil® tablets [prescribing information]. Parsippany, NJ: Teva; December 2022.
16. Nuvigil® tablets [prescribing information]. Parsippany, NJ: Teva; December 2022.