

PHARMACY POLICY STATEMENT

North Carolina Marketplace

DRUG NAME	Xyrem (sodium oxybate), Lumryz (sodium oxybate extended release) and Xywav (calcium, magnesium, potassium, and sodium oxybates)
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Xyrem, Lumryz and Xywav are central nervous system depressants indicated for narcolepsy associated with cataplexy or excessive daytime sleepiness in adults. Xyrem and Xywav are also approved in patients 7 years of age and older. Additionally, Xywav is approved for idiopathic hypersomnia for adults. The exact mechanism of action is unknown, but it's hypothesized the therapeutic effects work through the GABA_B actions during sleep at noradrenergic and dopaminergic neurons, as well as at thalamocortical neurons.

Narcolepsy is a chronic neurologic disorder involving dysregulation of the sleep/wake cycle. It is estimated about 50 per 100,000 people in the U.S. have narcolepsy. Idiopathic hypersomnia (IH) is a chronic neurological disorder that results in daytime sleepiness, frequently accompanied by long nocturnal or daytime sleep, unrefreshing sleep, difficulty in awakening, cognitive dysfunction, and autonomic symptoms. A less common condition than narcolepsy, there are approximately 20 to 50 cases per million of idiopathic hypersomnia.

Xyrem (sodium oxybate), Lumryz (sodium oxybate extended release) and Xywav (calcium, magnesium, potassium, and sodium oxybates) will be considered for coverage when the following criteria are met:

Idiopathic Hypersomnia – Xywav only

For **initial** authorization:

1. Member is 18 years old or older; AND
2. Medication must be prescribed by or in consultation with a neurologist or sleep specialist; AND
3. Member must have a diagnosis of idiopathic hypersomnia with the presence of at least **one** of the following:
 - a) MSLT (multiple sleep latency test) showing a mean sleep latency of ≤ 8 minutes; OR
 - b) Total 24-hour sleep time is ≥ 660 minutes (usually 12 to 14 hours) on 24-hour polysomnography or by wrist actigraphy in association with a sleep log; AND
4. Member has documentation of **ALL** of the following:
 - a) An MSLT showing fewer than two sleep-onset rapid eye movement periods (SOREMPs), or no SOREMPs if the REM sleep latency before polysomnogram is 15 minutes or less;
 - b) Daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months; AND
 - c) Baseline Epworth Sleepiness Scale (ESS); AND
 - d) At least 7 hours of sleep per night; AND
 - e) Absence of cataplexy; AND
5. Member has had a 60-day trial of modafinil; AND
6. Member has a 60-day trial of a stimulant medication (i.e., methylphenidate or dextroamphetamine); AND
7. Member is not using any alcohol or sedative hypnotic agents (such as zolpidem).
8. **Dosage allowed/Quantity limit:** Administer as a once or twice nightly regimen. QL: 540 mL/30 days

- a) Once nightly dosing: Initiate dosage at 3 g or less per night orally, as one dose. Titrate to effect in increments of up to 1.5g per night per week, up to 6g total nightly dose.
- b) Twice nightly dosing: Initiate dosage at 4.5g or less per night orally, divided into two doses. Titrate to effect in increments of up to 1.5g per night per week, up to 9g total nightly dose.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must show improvement or stabilized signs and symptoms of disease (ex. Improved score on the Epworth Sleepiness Scale and/or improved signs and symptoms of daytime sleepiness, etc.).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Narcolepsy with Excessive Daytime Sleepiness (EDS)

For **initial** authorization:

1. For Xyrem or Xywav, member is 7 years old or older; OR
2. For Lumryz, member is 18 years old or older; AND
3. Medication must be prescribed by or in consultation with a neurologist or sleep specialist; AND
4. Member has a diagnosis of narcolepsy with EDS confirmed by sleep studies: polysomnogram and multiple sleep latency test (MSLT); AND
5. Member has documentation of baseline Epworth Sleepiness Scale (ESS); AND
6. If member is 18 years of age and older:
 - a) Member has had a 30-day trial of BOTH of the following: Modafinil OR armodafinil AND Sunosi; AND
 - b) Member has had a 60-day trial of Wakix; OR
7. If member is less than 18 years of age:
 - a) Member has had a 30-day trial of modafinil (trial of a stimulant medication such as methylphenidate is also acceptable); AND
8. Member is not using any alcohol or sedative hypnotic agents (such as zolpidem).
9. **Dosage allowed/Quantity limit**:
 - a) Xyrem and Xywav: 9g per day (4.5g per dose). QL: 540 mL/30 days
 - b) Lumryz: 6 g to 9 g once per night. QL: 30 packets/30 days

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must show improvement or stabilized signs and symptoms of disease (ex. Improved score on the Epworth Sleepiness Scale and/or improved signs and symptoms of daytime sleepiness, etc.).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Narcolepsy with Cataplexy

For **initial** authorization:

1. For Xyrem or Xywav, member is 7 years old or older; OR
2. For Lumryz, member is 18 years old or older; AND
3. Medication must be prescribed by or in consultation with a neurologist or sleep specialist; AND
4. Member must have a diagnosis of narcolepsy with cataplexy confirmed by sleep studies: polysomnogram and multiple sleep latency test (MSLT); AND

5. Member has documentation of baseline Epworth Sleepiness Scale (ESS) and baseline frequency of cataplexy attacks (e.g. weekly rate); AND
6. Member has had a 30-day trial of one of the following: a tricyclic antidepressant (such as clomipramine), selective serotonin reuptake inhibitor (such as fluoxetine), serotonin-norepinephrine reuptake inhibitor (such as venlafaxine) or dextroamphetamine; AND
7. If member is 18 years of age and older: Member must have a 60-day trial an of Wakix; AND
8. Member is not using any alcohol or sedative hypnotic agents (such as zolpidem).
9. **Dosage allowed/Quantity limit:**
 - a) Xyrem and Xywav: 9g per day (4.5g per dose). QL: 540 mL/30 days
 - b) Lumryz: 6 g to 9 g once per night. QL: 30 packets/30 days

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization:**

1. Chart notes must show improvement or stabilized signs and symptoms of disease (ex. Decreased frequency and/or severity of cataplexy attacks, etc.).

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Xyrem (sodium oxybate), Lumryz (sodium oxybate extended release) and Xywav (calcium, magnesium, potassium, and sodium oxybates) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
05/26/2020	New policy for Xyrem created.
01/28/2021	Xywav added to policy. For cataplexy section: reduced trial of antidepressants from 2 to 1; added step through Wakix for adults.
11/15/2021	Transferred to new template. Added new section for idiopathic hypersomnia. Narcolepsy with EDS: For peds, emphasized modafinil as step therapy rather than a stimulant per the newest AASM guideline update; retained stimulant as an option.
05/18/2023	Added Lumryz; added references; removed attestation of lack of evidence of abuse, misuse or diversion, abstaining from alcohol or sedative hypnotics and lack of serious adverse effects from reauthorization criteria; added criterion to EDS for absence of hypnotic agents; added option of dextroamphetamine trial for cataplexy to align with evidence.

References:

1. Xywav [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2021.
2. Xyrem [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2023.
3. Lumryz [package insert]. Chesterfield, MO: Avadel CNS Pharmaceuticals, LLC; 2023.
4. American Academy of Sleep Medicine. International Classification of Sleep Disorders, 3rd ed. 2014.
5. Lecendreux M, Bruni O, Franco P, et al. Clinical experience suggests that modafinil is an effective and safe treatment for paediatric narcolepsy. Journal of Sleep Research. 2012;21(4):481-483.
6. Leher P, Falissard B. Multiple treatment comparison in narcolepsy: a network meta-analysis. Sleep. 2018;41(12). doi:10.1093/sleep/zsy185
7. Morgenthaler TI, Kapur VK, Brown TM, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin. Sleep. 2007;30(12):1705-1711.
8. Bogan RK, Thorpy MJ, Dauvilliers Y, et al. Efficacy and safety of calcium, magnesium, potassium, and sodium oxybates (lower-sodium oxybate [LXB]; JZP-258) in a placebo-controlled, double-blind, randomized withdrawal study in adults with narcolepsy with cataplexy [published online ahead of print, 2020 Oct 14]. Sleep. 2020

9. Barateau, L., & Dauvilliers, Y. (2019). Recent advances in treatment for narcolepsy. Therapeutic advances in neurological disorders.
10. Thorpy MJ, Bogan RK. Update on the pharmacologic management of narcolepsy: mechanisms of action and clinical implications. *Sleep Med.* 2020;68:97-109.
11. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2021;17(9):1881-1893. doi:10.5664/jcsm.9328
12. 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):1895-1945. doi:10.5664/jcsm.9326
13. Bassetti CLA, Kallweit U, Vignatelli L, et al. European guideline and expert statements on the management of narcolepsy in adults and children. *J Sleep Res.* 2021;30(6):e13387. doi:10.1111/jsr.13387

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