CareSource Rxinnovations

PHARMACY POLICY STATEMENT
Marketplace

DRUG NAME	Xyrem (sodium oxybate) and Xywav (calcium, magnesium, potassium, and sodium oxybates)
BILLING CODE	Must use valid NDC
BENEFIT TYPE	Pharmacy
SITE OF SERVICE ALLOWED	Home
STATUS	Prior Authorization Required

Xywav is a central nervous system depressant indicated for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy as well as idiopathic hypersomnia for adults. 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. The exact mechanism of action of Xywav 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.

Xyrem (sodium oxybate) 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;
   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;
4. Documentation of a 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;
5. Documentation of daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months; AND
6. Baseline Epworth score has been submitted in chart notes;
7. Member does NOT have documentation of cataplexy; AND
8. Member has a previous trial of modafinil for at least 60 days which was ineffective, not tolerated, or contraindicated; AND
9. Member has documentation of at least 7 hours of sleep per night; AND
10. Member has a previous trial of a stimulant medication (i.e., methylphenidate or dextroamphetamine) for at least 60 days which was ineffective, not tolerated, or contraindicated.
11. **Dosage allowed/Quantity limit:** Administer as a once or twice nightly regimen.
    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.

QL: 540 mL/30 days

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

For **reauthorization**:
Xywav will be reauthorized when chart notes show ALL of the following:
1. Chart notes must show the member has an improved score on the Epworth Sleepiness Scale and/or improved signs and symptoms of daytime sleepiness; AND
2. Member must continue to abstain from alcohol and any sedative hypnotic agents; AND
3. Member tolerates therapy and does not experience unmanageable or severe adverse effects; AND
4. Chart notes must not reveal any evidence of abuse, misuse, or diversion.

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. Member is 7 years old or older; AND
2. Medication must be prescribed by or in consultation with a neurologist or sleep specialist; AND
3. Member has a diagnosis of narcolepsy with EDS confirmed by sleep studies: polysomnogram and MSLT (multiple sleep latency test); AND
4. Member's current score on the Epworth Sleepiness Scale (ESS) is documented in chart notes; AND
5. a) Age 18 years or older: Member has had a compliant trial and failure for at least 30 days for each of the following at maximally tolerated doses: modafinil OR armodafinil, AND Sunosi; AND at least 60 days of Wakix, unless not tolerated or contraindicated; OR
   b) Less than 18 years of age: Member has had a compliant trial and failure of modafinil for at least 30 days (trial of a stimulant medication such as methylphenidate is also acceptable); AND
6. Member is not using any alcohol or sedative hypnotic agents (such as zolpidem).
7. **Dosage allowed/Quantity limit:** 9g per day (4.5g per dose).
   QL: 540 mL/30 days

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

For **reauthorization**:
1. Chart notes must show the member has an improved score on the Epworth Sleepiness Scale and/or improved signs and symptoms of daytime sleepiness; AND
2. Member must continue to abstain from alcohol and any sedative hypnotic agents; AND
3. Member tolerates therapy and does not experience unmanageable or severe adverse effects; AND
4. Chart notes must not reveal any evidence or concerns of abuse, misuse, or diversion.

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

Narcolepsy with Cataplexy

For **initial** authorization:
1. Member is 7 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 narcolepsy with cataplexy confirmed by sleep studies: polysomnogram and MSLT (multiple sleep latency test); AND
4. Member's current score on the Epworth Sleepiness Scale and baseline frequency of cataplexy attacks (e.g. weekly rate) must be documented; AND
5. Member must have, unless specifically contraindicated, a compliant trial and failure of at least one of the following cataplexy treatments for no less than 30 days: A tricyclic antidepressant (such as clomipramine), selective serotonin reuptake inhibitor (such as fluoxetine), or serotonin-norepinephrine reuptake inhibitor (such as venlafaxine); AND
6. Members 18 years of age and older must have a trial and failure of Wakix for at least 60 days; AND

7. Member is not using any alcohol or sedative hypnotic agents (such as zolpidem).
8. **Dosage allowed/Quantity limit:** 9g per day (4.5g per dose).
   QL: 540 mL/30 days

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

For **reauthorization**:
1. Chart notes must show decreased frequency and/or severity of cataplexy attacks; AND
2. Member must continue to abstain from alcohol and any sedative hypnotic agents; AND
3. Member tolerates therapy and does not experience unmanageable or severe adverse effects; AND
4. Chart notes must not reveal any evidence of abuse, misuse, or diversion.

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

CareSource considers Xyrem (sodium oxybate) 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.

References:

1. Xywav [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2021.
2. American Academy of Sleep Medicine. International Classification of Sleep Disorders, 3rd ed. 2014.
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5. Lehert P, Falissard B. Multiple treatment comparison in narcolepsy: a network meta-analysis. Sleep. 2018;41(12). doi:10.1093/sleep/zsy185
6. 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.
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8. Barateau, L., & Dauvilliers, Y. (2019). Recent advances in treatment for narcolepsy. Therapeutic advances in neurological disorders.
9. Thorpy MJ, Bogan RK. Update on the pharmacologic management of narcolepsy: mechanisms of action and clinical implications. Sleep Med. 2020;68:97-109.
10. 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
11. 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

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