Xywav (calcium, magnesium, potassium, and sodium oxybates)

Summary

Narcolepsy is a chronic neurological disorder characterized by excessive daytime sleepiness (EDS) and abnormal rapid eye movement (REM) sleep manifestations, including cataplexy, sleep paralysis, and hypnagogic hallucinations. It affects approximately 1 in 2,000 people in the United States. Idiopathic hypersomnia (IH) is a neurological sleep disorder characterized by excessive daytime sleepiness despite adequate or prolonged nighttime sleep.

First-line treatments for narcolepsy typically include central nervous system stimulants (e.g., modafinil, armodafinil, methylphenidate, amphetamines) for EDS, and sodium oxybate or antidepressants (e.g., SSRIs, SNRIs, TCAs) for cataplexy. For idiopathic hypersomnia, similar wake-promoting medications are used as first-line treatments.

Xywav (calcium, magnesium, potassium, and sodium oxybates) is a central nervous system depressant approved by the FDA for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy, and for the treatment of idiopathic hypersomnia in adults. It offers a lower-sodium alternative to Xyrem (sodium oxybate) and is typically considered after other treatments have failed or are contraindicated.

Definitions

"**Cataplexy**" refers to a sudden, transient episode of muscle weakness accompanied by full conscious awareness, typically triggered by emotions such as laughing, crying, or terror.

"**Excessive daytime sleepiness (EDS)**" is the inability to stay awake and alert during the day, resulting in unintended lapses into drowsiness or sleep.

"**Hypnagogic hallucinations**" are vivid, often frightening, dreamlike experiences that occur while falling asleep.

"Hypocretin-1" is a natural chemical in the brain that helps regulate wakefulness.

"**Idiopathic hypersomnia (IH)**" is a neurological disorder characterized by excessive daytime sleepiness that is not caused by disturbed sleep at night, other medical conditions, or medications.

"**Multiple Sleep Latency Test (MSLT)**" is a sleep study that measures how quickly a person falls asleep during the day and whether they enter rapid eye movement (REM) sleep.

"**Narcolepsy**" is a chronic neurological disorder that affects the brain's ability to control sleep-wake cycles.

"Polysomnography (PSG)" is a sleep study used to diagnose sleep disorders by measuring certain components such as brain activity, oxygen levels, heart rate, breathing, eye movements, and leg movements.

"Sleep latency" is the amount of time it takes to fall asleep.

"**Sleep-onset REM periods (SOREMPs)**" are periods of rapid eye movement sleep that occur within 15 minutes of falling asleep, which are characteristic of narcolepsy.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Xywav (calcium, magnesium, potassium, and sodium oxybates)** medically necessary when **ALL** of the following criteria are met:

1. The medication is prescribed by or in consultation with a sleep medicine specialist, neurologist, psychiatrist, or pulmonologist with expertise in treating sleep disorders***; AND***
2. The member meets the age requirement for the intended use:
    a. For treatment of cataplexy or excessive daytime sleepiness (EDS) in narcolepsy - the member is 7 years of age or older***; or***
    b. For treatment of idiopathic hypersomnia (IH) - the member is 18 years of age or older***; AND***
3. The member has a diagnosis of narcolepsy or idiopathic hypersomnia that has been confirmed by sleep lab testing or documented clinical symptoms:
    a. For narcolepsy - excessive daytime sleepiness (EDS) persisting for at least 3 months **AND** at least **ONE** of the following:
        i. Cataplexy episodes (for narcolepsy type 1)***; or***
        ii. Hypocretin-1 (orexin A) deficiency (≤110 pg/mL or <1/3 of mean values of healthy individuals tested using the same standardized assay)***; or***
        iii. Nocturnal sleep polysomnography showing rapid eye movement (REM) sleep latency ≤ 15 minutes, or a Multiple Sleep Latency Test (MSLT) showing a mean sleep latency ≤ 8 minutes and ≥ 2 sleep-onset REM periods (SOREMPs). A SOREMP within 15 minutes of sleep onset on the preceding nocturnal polysomnography may replace one of the SOREMPs on the MSLT***; or***
    b. For idiopathic hypersomnia - excessive daytime sleepiness (EDS) persisting for at least 3 months **AND** a Multiple Sleep Latency Test (MSLT) showing a mean sleep latency of ≤ 8 minutes and fewer than 2 sleep-onset REM periods (SOREMPs), or no SOREMPs if the REM latency on the preceding polysomnogram was ≤ 15 minutes***; AND***
4. The member has tried and failed prior treatments as follows:
    a. For members 18 years of age and older with narcolepsy, the member has tried and failed, or has a contraindication to, **ALL** of the following:
        i. Sunosi (solriamfetol)***; and***
        ii. Lumryz (sodium oxybate)***; and***
        iii. Wakix (pitolisant)***; or***

b. For members 7 to 17 years of age with narcolepsy and excessive daytime sleepiness (EDS), the member has tried and failed, or has a contraindication to, **ALL** of the following:
    i. Wakix (pitolisant)***; and***
    ii. Lumryz (sodium oxybate); ***or***
c. For members 7 to 17 years of age with narcolepsy and cataplexy, **the member has tried and failed, or has a contraindication to, Lumryz (sodium oxybate)**; ***or***
d. For adults with idiopathic hypersomnia, the member is unable to use, or has adequately tried and failed at least **THREE** (3) of the following for at least 30 days duration each:
    i. amphetamine-dextroamphetamine; ***and/or***
    ii. dextroamphetamine; ***and/or***
    iii. methylphenidate; ***and/or***
    iv. armodafinil; ***and/or***
    v. modafinil; ***AND***

5. The member does **NOT** have **ANY** of the following:
    a. Succinic semialdehyde dehydrogenase (SSADH) deficiency***; or***
    b. Documentation indicating concomitant use with, or inability to abstain from, any of the following while taking Xywav:
        i. Alcohol (e.g., beer, wine, whisky)***; or***
        ii. Sedative hypnotics (e.g., alprazolam, diazepam, lorazepam, zolpidem)***; or***
        iii. Xyrem, Lumryz, or other sodium oxybate products***; or***
    c. A condition that better explains the hypersomnolence and/or MSLT findings, such as:
        i. Insufficient sleep***; or***
        ii. Obstructive sleep apnea***; or***
        iii. Delayed sleep phase disorder***; or***
        iv. The effect of medication or substances or their withdrawal***; AND***
6. Xywav is being prescribed at a dose and frequency that is within FDA approved labeling **OR** is supported by compendia or evidence-based published dosing guidelines for the requested indication.

If the above prior authorization criteria are met, the requested product will be authorized for 12 months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if the member has recent (within the last 3 months) clinical chart documentation demonstrating **ALL** of the following criteria:

1. The member has experienced a positive clinical response to Xywav therapy as demonstrated by a reduction in symptoms of cataplexy, EDS, or IH; ***AND***
2. The member continues to abstain from alcohol and sedative hypnotics; ***AND***
3. Xywav will not be used in combination with Xyrem, Lumryz, or other sodium oxybate products; ***AND***
4. Xywav continues to be prescribed at a dose and frequency that is within FDA approved labeling **OR** is supported by compendia or evidence-based published dosing guidelines for the requested indication.

Experimental or Investigational / Not Medically Necessary

Xywav (calcium, magnesium, potassium, and sodium oxybates) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- When used in combination with alcohol, sedative hypnotics, or other medications containing sodium oxybate, gamma-hydroxybutyrate (GHB), or GHB precursors.
- When used in members with succinic semialdehyde dehydrogenase deficiency, a rare inborn error of metabolism.
- For members under 7 years of age, safety and efficacy have not been established in this pediatric population.

References

1. Aurora RN, Lamm CI, Zak RS, Kristo DA, Bista SR, Rowley JA, Casey KR. Practice parameters for the non-respiratory indications for polysomnography and multiple sleep latency testing for children. Sleep. 2012 Nov 1;35(11):1467-73. doi: 10.5665/sleep.2190. PMID: 23115395; PMCID: PMC3466793.
2. Howell M, Avidan AY, Foldvary-Schaefer N, Malkani RG, During EH, Roland JP, McCarter SJ, Zak RS, Carandang G, Kazmi U, Ramar K. Management of REM sleep behavior disorder: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2023 Apr 1;19(4):759-768. doi: 10.5664/jcsm.10424. PMID: 36515157; PMCID: PMC10071384.
3. Maski K, Trotti LM, Kotagal S, Robert Auger R, Rowley JA, Hashmi SD, Watson NF. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2021 Sep 1;17(9):1881-1893. doi: 10.5664/jcsm.9328. PMID: 34743789; PMCID: PMC8636351.

4. Xywav (calcium, magnesium, potassium, and sodium oxybates) [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals Inc; April 2023.

Clinical Guideline Revision / History Information

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