xywav®
(calcium, magnesium, potassium, and sodium oxybates) oral solution CIII

Guide to Completing a Prior Authorization

Indication for Idiopathic Hypersomnia in Adults

Having the right information before completing a prior authorization (PA) may help healthcare providers navigate the process and avoid delays. This guide highlights:

- Common PA criteria for the idiopathic hypersomnia indication for XYWAV® (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII, 0.5 g/mL total salts (equivalent to 0.413 g/mL of oxybate) by large national health plans[a,b]
- The PA appeals process

[a]Based on the AASM ICSD-3 Guidelines.
[b]Specific PA criteria presented on page 2 may vary by health plan; therefore, please refer to the health plan's PA criteria or contact the health plan for additional information.
AASM=American Academy of Sleep Medicine; ICSD-3=International Classification of Sleep Disorders, Third Edition.

Indications and Usage

XYWAV is indicated for the treatment of idiopathic hypersomnia in adults.

Important Safety Information

WARNING: CENTRAL NERVOUS SYSTEM DEPRESSION and ABUSE AND MISUSE.

- **Central Nervous System Depression**
  XYWAV is a CNS depressant. Clinically significant respiratory depression and obtundation may occur in patients treated with XYWAV at recommended doses. Many patients who received XYWAV during clinical trials in idiopathic hypersomnia (IH) were receiving CNS stimulants.
- **Abuse and Misuse**
  The active moiety of XYWAV is oxybate or gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB, 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 and abuse and misuse, XYWAV is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the XYWAV and XYREM REMS.

Contraindications

XYWAV is contraindicated in combination with sedative hypnotics or alcohol and in patients with succinic semialdehyde dehydrogenase deficiency.

Please see additional Important Safety Information on next page and full Prescribing Information, including BOXED Warning.

PA Approval Criteria

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Common policy criteria required by national health plans for the idiopathic hypersomnia indication for XYWAV[1]:

- ☐ Daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for ≥3 months
- ☐ Cataplexy is absent
- ☐ MSLT shows <2 SOREMPs ***OR*** no SOREMPs if the REM latency on the preceding PSG was ≤15 minutes
- ☐ Presence of at least 1 of the following:
  1. MSLT shows a mean sleep latency of ≤8 minutes
  2. Total 24-hour sleep time is ≥660 minutes (typically 12–14 hours) on 24-hour PSG monitoring,[a] or by wrist actigraphy in association with a sleep log[b]
- ☐ Insufficient sleep syndrome is ruled out[c]
- ☐ The hypersomnolence and/or MSLT findings are not better explained by another sleep disorder, other medical or psychiatric disorder, or use of drugs or medication

Reauthorization Criteria

Treatment with XYWAV can be continued based on the following criteria[2,3]:

- ☐ Met initial diagnostic criteria noted above
- ☐ Demonstrated a reduction in symptoms of EDS associated with therapy

When submitting a PA at initial fill, or a reauthorization request, it is important to include documentation that the patient has met the diagnostic criteria (eg, chart notes; lab or test results). At reauthorization, some health plans may also review test results for evidence of symptomatic improvement.[2,4]

Did you still receive a denial? Please see the next page for more information about appeals.

[a]Performed after correction of chronic sleep deprivation. [b]Averaged over at least 7 days with unrestricted sleep. [c]If deemed necessary, by lack of improvement of sleepiness after an adequate trial of increased nocturnal time in bed, preferably confirmed by at least a week of wrist actigraphy.[1]

EDS=excessive daytime sleepiness; MSLT=Multiple Sleep Latency Test; PSG=polysomnography/polysomnographic; REM=rapid eye movement; SOREMPs=sleep onset REM periods.

Important Safety Information (cont.)

Warnings and Precautions

- CNS Depression: Use caution when considering the concurrent use with other CNS depressants. If concurrent use is required, consider dose reduction or discontinuation of one or more CNS depressants (including XYWAV). Consider interrupting XYWAV treatment if short-term opioid use is required. After first initiating treatment and until certain that XYWAV does not affect them adversely, caution patients against hazardous activities requiring complete mental alertness or motor coordination such as operating hazardous machinery, including automobiles or airplanes. Also caution patients against these hazardous activities for at least 6 hours after taking XYWAV. Patients should be queried about CNS depression-related events upon initiation of XYWAV therapy and periodically thereafter.
- Abuse and Misuse: XYWAV is a Schedule III controlled substance. The rapid onset of sedation, coupled with the amnestic features of GHB particularly when combined with alcohol, has proven to be dangerous for the voluntary and involuntary user (eg, assault victim).

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PA Appeals Process

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Even if a PA is denied, your patient may still be able to access the medicine they need by submitting an appeal. In many cases, the health plan might simply need additional information before approving XYWAV. There are many aspects to submitting an appeal and responding to a denial, but the process generally follows the steps shown below.

3 LEVELS OF APPEAL

1. **Reconsideration:** Health plan denies claim based on clinical or policy-related reasons.[5]

   Response: *Often requires HCP's office to send additional clinical information[a] or have a discussion with a board-certified peer appointed by the payer; a letter of medical necessity may also be required.*

2. **Medical Director Review:** Proof is needed to show the request should be accepted within the coverage guidelines.[5]

   Response: *A medical director of the patient's health plan who was not involved in the claim decision conducts a review.*

3. **Independent External Review:** Reconsideration does not result in approval.[5]

   Response: *HCP's office requests an independent, third-party review in collaboration with a physician who is board-certified in the same specialty as the patient's HCP.*

RESPONDING TO A DENIAL IN 3 STEPS

1. **First, find out why the health insurance claim was denied[6]**
   - Review the health plan's explanation of benefits and medical policy guidelines[6]
     - Have the PA approval criteria been met?[2,4,7]
     - Have required documents been provided (eg, test results [eg, PSG, MSLT, total sleep time], prior medications tried/failed, office notes)?[2,4]

2. **Next, contact the health plan to determine the number of days within which an appeal must be submitted[8]**
   - The deadline to appeal is usually 30, 60, or 180 days after receiving the denial

3. **Finally, keep the original documents and submit copies to the patient's health plan[8]**
   - At the end of the appeals process, the health plan must provide a written decision

[a]Consider including information such as blood pressure readings, history of cardiovascular issues, or history of hypertension, if applicable to the patient.

HCP=healthcare provider.

Important Safety Information (cont.)

Warnings and Precautions (cont.)

- Respiratory Depression and Sleep-Disordered Breathing: XYWAV may impair respiratory drive, especially in patients with compromised respiratory function. In overdoses of oxybate and with illicit use of GHB, life-threatening respiratory depression has been reported. Increased apnea and reduced oxygenation may occur with XYWAV administration in adult and pediatric patients. A significant increase in the number of central apneas and clinically significant oxygen desaturation may occur in patients with obstructive sleep apnea treated with XYWAV. Prescribers should be aware that sleep-related breathing disorders tend to be more prevalent in obese patients, in men, in postmenopausal women not on hormone replacement therapy, and among patients with narcolepsy.

Please see additional Important Safety Information on next page and full Prescribing Information, including BOXED Warning.

If you require additional assistance or information, please contact your Jazz Access and Reimbursement Manager. You can also call a Reimbursement Specialist with the Certified Pharmacy at 1-866-997-3688.

Important Safety Information (cont.)

Warnings and Precautions (cont.)

- Depression and Suicidality: In the pivotal clinical trial in adult patients with IH, depression and depressed mood were reported in patients treated with XYWAV. In most cases, no change in XYWAV treatment was required. Two suicides and two attempted suicides occurred in adult clinical trials with oxybate (same active moiety as XYWAV). One patient experienced suicidal ideation and two patients reported depression in a pediatric clinical trial with oxybate. **Monitor patients for the emergence of increased depressive symptoms and/or suicidality while taking XYWAV, which require careful and immediate evaluation.**
- Other Behavioral or Psychiatric Adverse Reactions: Monitor patients for impaired motor/cognitive function or the emergence of or increase in anxiety and/or confusion. The emergence or increase in the occurrence of behavioral or psychiatric events in patients taking XYWAV should be carefully monitored.
- Parasomnias: In pivotal clinical trials, parasomnias including sleepwalking were reported in adult patients treated with XYWAV. Parasomnias, including sleepwalking, also have been reported in postmarketing experience with sodium oxybate. Episodes of sleepwalking should be fully evaluated and appropriate interventions considered.

Most Common Adverse Reactions

In the adult clinical trials, in patients with IH, the most common adverse reactions occurring in ≥5% of XYWAV-treated patients were nausea, headache, anxiety, dizziness, insomnia, decreased appetite, hyperhidrosis, vomiting, dry mouth, diarrhea, fatigue, somnolence, parasomnia, and tremor.

Please see full Prescribing Information, including BOXED Warning.

For more information on XYWAV, visit www.xywavhcp.com.

References: 1. American Academy of Sleep Medicine. *International Classification of Sleep Disorders*, 3rd ed. 2014. **2.** UnitedHealthcare Pharmacy clinical pharmacy programs. UnitedHealthcare website. www.uhcprovider.com/content/dam/provider/docs/public/prior-auth/drugs-pharmacy/commercial/r-z/PA-Notification-Xyrem.pdf. Updated February 1, 2022. Accessed October 28, 2022. **3.** Xywav™ (calcium, magnesium, potassium, and sodium oxybates) pharmacy coverage program. Humana website. http://apps.humana.com/tad/tad_new/Search.aspx?criteria=xywav&searchtype=freetext&policyType=both. Accessed October 28, 2022. **4.** Specialty pharmacy clinical policy bulletins. Subject: Xywav 4045-A SGM P2021b. Aetna website. https://www.aetna.com/products/rxnonmedicare/data/2022/Xywav_4045-A_SGM_P2021b.html. Updated May 14, 2022. Accessed October 28, 2022. **5.** A patient's guide to navigating the insurance appeals process. Patient Advocate Foundation website. www.patientadvocate.org/wp-content/uploads/Navigating-the-insurance-appeals-guide-pages.pdf. Accessed October 28, 2022. **6.** Kasperowicz L. Tips for appealing a denied health insurance claim. Insurance.com website. https://www.insurance.com/health-insurance/coverage/appeal-a-health-insurance-claim-denial.html. Updated July 18, 2022. Accessed October 28, 2022. **7.** Oxybate prior authorization request. Prime Therapeutics website. https://www.myprime.com/content/dam/prime/memberportal/forms/AuthorForms/BCBSND/Commercial/ND_Oxybate_PA.pdf. July 2022. Accessed October 28, 2022. **8.** Internal appeals. Healthcare.gov website. https://www.healthcare.gov/appeal-insurance-company-decision/internalappeals/. Accessed October 28, 2022.

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