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

XYWAV Prescriber Checklist

Learn more about XYWAV, the first and only FDA-approved treatment for both narcolepsy and idiopathic hypersomnia (IH).[1-4]

Inside: discover how to prescribe XYWAV for your patients.

Learn about enrolling your patients in the XYWAV and XYREM REMS, how to complete and submit the Prescription Form, and more.

INDICATIONS AND USAGE

XYWAV® (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL total salts (equivalent to 0.413 g/mL of oxybate) is indicated 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 (IH) 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 narcolepsy and idiopathic hypersomnia 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.

Please see additional Important Safety Information on the following pages and accompanying full Prescribing Information, including BOXED Warning.

To enroll and prescribe XYWAV for your patients:

STEP 1: Enroll in the REMS

Before you prescribe XYWAV for your patients, **you and your patients must be enrolled in the XYWAV and XYREM REMS.[1,5] HCPs can enroll themselves and their patients at XYWAVXYREMREMS.com, OR, print, sign, and**

1. Fax to the XYWAV and XYREM REMS: 1-866-470-1744 (toll-free)
2. OR mail to the XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589
3. OR scan and email to the XYWAV and XYREM REMS at ESSDSPrescribers@express-scripts.com

Note: Prescribers and patients who are actively enrolled in the XYREM REMS are not required to re-enroll in the XYWAV and XYREM REMS.

STEP 2: Complete the Prescription Form

- The XYWAV Prescription Form or XYREM Prescription Form is provided through Jazz Pharmaceuticals and is available to download online at XYWAVXYREMREMS.com
- If a patient who has been taking XYREM is switching to XYWAV, a XYWAV Prescription Form is required to be filled out and sent to the Certified Pharmacy
  - A patient cannot have overlapping and active prescriptions of XYWAV and XYREM at the same time

A Prescription Form is also required for oxybate-naïve patients. Refer to the XYWAV and XYREM Prescriber Brochure or full Prescribing Information for further information.

STEP 3: Submit the Prescription Form

Download the Prescription Form via XYWAVXYREMREMS.com and print, sign, and:

1. Fax to the XYWAV and XYREM REMS: 1-866-470-1744 (toll-free)
2. OR mail to the XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589

STEP 4: Tell patients to expect a call from the Certified Pharmacy

- To help guide them through the process, patients should expect 2 calls from the Certified Pharmacy:
  - A welcome call from a JazzCares® Nurse Case Manager to learn more about program offerings, support, and reimbursement
  - A REMS Counseling call with a pharmacist to go over safety Information and answer any additional questions prior to the first shipment of XYWAV (for new patients or restart patients who have been off of therapy for 6 months or more)
- To help encourage patients to answer these calls, let them know they should add the Certified Pharmacy's number (1-866-997-3688) to their contact list
- Also, encourage your patients to sign the JazzCares Consent for service eligibility at JazzCaresConsent.com

STEP 5: Set your patients up for success

- Ensure your patients have the Getting Started on XYWAV brochure and encourage your patients to register for myWAV at myWAV.com, your patients' digital one-stop shop for personalized support and motivation
- With myWAV, your patient will also get tools to help them start their treatment, set personalized notifications, and more

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For patients transitioning from XYREM® (sodium oxybate) oral solution to XYWAV

Smaller bottle. Same amount of medicine.

Although the 6-oz XYWAV bottle is smaller than the 8-oz XYREM bottle, both bottles contain the same volume of medicine: 180 mL.[1,6]

JazzCares® is your partner in supporting your patients throughout their treatment journey. Our program is designed to support your patients' needs from day 1. Visit www.JazzCares.com/Xywav to learn more.

Important Safety Information (cont'd)

Contraindications

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

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 XYW AV). 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 Ill 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).

- 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.

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Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

- Depression and Suicidality: In clinical trials in adult patients with narcolepsy and 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 clinical trials, parasomnias including sleepwalking were reported in adult patients treated with XYWAV. Parasomnias, including sleepwalking, also have been reported in a pediatric clinical trial with sodium oxybate (same active moiety as XYWAV) and in postmarketing experience with sodium oxybate. Episodes of sleepwalking should be fully evaluated and appropriate interventions considered.

Most Common Adverse Reactions

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

In the pediatric clinical trial with XYREM (same active moiety as XYWAV) in patients 7 years of age and older with narcolepsy, the most common adverse reactions (≥5%) were nausea (20%), enuresis (19%), vomiting (18%), headache (17%), weight decreased (13%), decreased appetite (9%), dizziness (8%), and sleepwalking (6%). The safety profile in pediatric patients with XYWAV is expected to be similar to that of adult patients treated with XYWAV and to that of pediatric patients treated with XYREM.

Please see accompanying full Prescribing Information, including BOXED Warning.

References:

1. XYWAV® (calcium, magnesium, potassium, and sodium oxybates). Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.
2. Thorpy MJ. Recently approved and upcoming treatments for narcolepsy. *CNS Drugs*. 2020;34(1):9-27.
3. 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. *Sleep*. 2021;44(3):zsaa206.
4. US Department of Health and Human Services, Food and Drug Administration. FDA news release: FDA grants first of its kind indication for chronic sleep disorder treatment. https://www.fda.gov/news-events/press-announcements/fda-grants-first-its-kind-indication-chronic-sleep-disorder-treatment. Published August 12, 2021. Accessed April 27, 2022.
5. XYWAV and XYREM REMS Document. NDA 21196; NDA 212690. XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) and XYREM® (sodium oxybate). Palo Alto, CA: Jazz Pharmaceuticals, Inc. Approved 02/2015. https://www.accessdata.fda.gov/Scripts/Cder/Rems/Index.cfm?event=IndvRemsDetails.page&REMS=345. Accessed September 15, 2020.
6. XYREM® (sodium oxybate). Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

Jazz Pharmaceuticals

US-XYW-2000149 Rev0822

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