xywav®

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

XYWAV IS THE

FIRST & ONLY FDA-APPROVED TREATMENT

FOR ADULTS LIVING WITH

IDIOPATHIC HYPERSOMNIA (IH)[1]

Could XYWAV be right for your adult patients with idiopathic hypersomnia?
To find out, see the ICSD-3 criteria and patient profile on the following pages.

INDICATION 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 idiopathic hypersomnia (IH) in adults.

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 throughout and full Prescribing Information, including BOXED Warning.

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Let's take a look at your adult patients with idiopathic hypersomnia

The International Classification of Sleep Disorders (3rd Edition, ICSD-3) is an important tool to help determine if XYWAV is right for them

Diagnosing idiopathic hypersomnia can be challenging for two main reasons[2]:

- Excessive Daytime Sleepiness (EDS) is a core feature of multiple sleep disorders
- There is currently no validated biomarker for idiopathic hypersomnia

The ICSD-3 helps objectively diagnose patients, and provides important information to consider when developing a treatment plan.

For a diagnosis of idiopathic hypersomnia, the following must be met[3]

ICD-10-CM codes: G47.11 (with long sleep), G47.12 (without long sleep)

EDS daily for ≥3 months

Cataplexy is **NOT** present

MSLT shows <2 or no SOREMPs if the REM latency on the preceding PSG was ≤15 minutes

Insufficient sleep syndrome is ruled out

At least one of the following:

- MSLT shows a mean sleep latency of ≤8 minutes
- Total 24-hour sleep time is ≥660 minutes (typically 12–14 hours) on 24-hour PSG monitoring (performed after correction of chronic sleep deprivation), or by wrist actigraphy in association with a sleep log (averaged over at least 7 days with unrestricted sleep)

Hypersomnolence and/or MSLT findings are not better explained by another sleep disorder, other medical or psychiatric disorders, or use of drugs or medication

Additional supportive clinical features include[3]:

- Severe and prolonged sleep inertia (difficulty waking with repeated returns to sleep, irritability, automatic behavior and confusion)
- Long, unrefreshing naps (>1 hour)
- High sleep efficiency (≥90%) on the preceding PSG

Think XYWAV may be right for your adult patients with idiopathic hypersomnia?
Visit **XYWAVHCP.com/START** to find out how to get them started.

EDS=Excessive Daytime Sleepiness, MSLT=Multiple Sleep Latency Test, PSG=polysomnography, REM=Rapid Eye Movement, SOREMP=Sleep-Onset Rapid Eye Movement Period.

Important Safety Information (cont'd)

Warnings and Precautions

Central Nervous System Depression

The concurrent use of XYWAV with other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptic drugs, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death. If use of these CNS depressants in combination with XYWAV is required, dose reduction or discontinuation of one or more CNS depressants (including XYWAV) should be considered. In addition, if short-term use of an opioid (eg, post- or perioperative) is required, interruption of treatment with XYWAV should be considered.

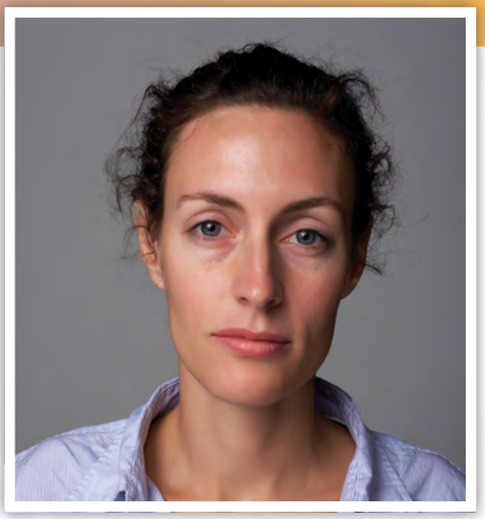
After first initiating treatment and until certain that XYWAV does not affect them adversely (eg, impair judgment, thinking, or motor skills), caution patients against hazardous activities requiring complete mental alertness or motor coordination such as operating hazardous machinery, including automobiles 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.

Please see additional Important Safety Information throughout and full Prescribing Information, including BOXED Warning.

Meet Theresa

Diagnosed with idiopathic hypersomnia and being treated with a wake-promoting agent (WPA), but still struggling with her symptoms

"My doctor said the only available medications at the time were either stimulants or "WPAs", and we decided on the latter together. Unfortunately, I still need help waking up in the morning. ***I also still have trouble concentrating and feel tired throughout the day."***



Actor pictured.

Age: 38 | **Sex:** Female | **BMI (kg/m²):** 19 | **Insurance:** Commercial

Case History:
Diagnosed by a sleep specialist 8 months ago with an MSLT that showed <2 SOREMPs, and a mean sleep latency of 7 minutes, but recalls experiencing symptoms as early as her mid-20s.

Excluded causes of EDS:

- Narcolepsy Type 1 due to absence of cataplexy
- Insufficient sleep syndrome
- Sleep apnea
- Other medical or psychiatric disorders
- Use of drugs or medications that can cause sleepiness

Treatment History:

- Lifestyle changes and sleep hygiene
- Modafinil, 400 mg, QD

Chief Complaint:

- Patient is unsatisfied with the symptom control of her current treatment.
- Patient still has trouble getting up in the morning, stating that she has to hit snooze 5-6 times or have her spouse help her wake up and get out of bed in order to start her day

XYWAV is approved as the first and only treatment option for adults with idiopathic hypersomnia, so whether your patients have started on other treatments or not, you can consider XYWAV for them.[1]

Theresa's doctor asked the following key questions to confirm that her current medication was insufficient in treating her symptoms of idiopathic hypersomnia

1. **Despite sleeping as much as you can at night, do you still feel tired or unrested?**
2. **Is it extremely difficult to wake up in the morning without several alarms or the help of someone else?**
3. **Do you struggle to function either physically or intellectually throughout the day?[5]**
4. **Do you wake up feeling unrefreshed from naps?**

Since Theresa answered "yes" to the majority of these questions, her doctor decided it was time to consider XYWAV. XYWAV is different from other treatment options–it's taken at night to help treat multiple symptoms of idiopathic hypersomnia during the day.*[1,6]

*The exact way XYWAV works is unknown.

Find out how you can get your patients started on XYWAV.
Visit XYWAVHCP.com/START

Important Safety Information (cont'd)

Abuse and Misuse

XYWAV is a Schedule III controlled substance. The active moiety of XYWAV is oxybate, also known as gamma-hydroxybutyrate (GHB), a Schedule I controlled substance. Abuse 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. 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). Physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely.

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Important Safety Information (cont'd)

XYWAV and XYREM REMS

- Because of the risks of central nervous system depression and abuse and misuse, XYWAV is available only through a restricted distribution program called the XYWAV and XYREM REMS.

Notable requirements of the XYWAV and XYREM REMS include the following:

- Healthcare Providers who prescribe XYWAV are specially certified
- XYWAV will be dispensed only by the central pharmacy that is specially certified
- XYWAV will be dispensed and shipped only to patients who are enrolled in the XYWAV and XYREM REMS with documentation of safe use

Further information is available at www.XYWAVXYREMREMS.com or 1-866-997-3688.

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.

Depression and Suicidality

In Study 2, the randomized-withdrawal clinical trial in adult patients with idiopathic hypersomnia (n=154), depression and depressed mood were reported in 1% and 3%, respectively, of patients treated with XYWAV. All patients continued XYWAV treatment.

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. These events occurred in patients with and without previous histories of depressive disorders. The emergence of depression in patients treated with XYWAV requires careful and immediate evaluation. Monitor patients for the emergence of increased depressive symptoms and/or suicidality while taking XYWAV.

Other Behavioral or Psychiatric Adverse Reactions

In Study 2, confusion and anxiety occurred in 3% and 16% of patients with idiopathic hypersomnia, respectively. One patient in Study 2 experienced visual hallucinations, which led to discontinuation of XYWAV.

Other neuropsychiatric reactions reported with oxybate (same active moiety as XYWAV) in adult or pediatric clinical trials and in the postmarketing setting include hallucinations, paranoia, psychosis, aggression, agitation, confusion, and anxiety. The emergence or increase in the occurrence of behavioral or psychiatric events in patients taking XYWAV should be carefully monitored.

Parasomnias

Parasomnias can occur in patients taking XYWAV.

In Study 2, parasomnias including sleepwalking were reported in 5% of adult patients with idiopathic hypersomnia treated with XYWAV.

Parasomnias, including sleepwalking, have been reported in postmarketing experience with sodium oxybate (same active moiety as XYWAV).

Episodes of sleepwalking should be fully evaluated and appropriate interventions considered.

Most Common Adverse Reactions

In Study 2, 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 additional Important Safety Information throughout and full Prescribing Information, including BOXED Warning.

References: 1. XYWAV® (calcium, magnesium, potassium, and sodium oxybates). Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **2.** Trotti LM. Idiopathic Hypersomnia. *Sleep Med Clin.* 2017;12(3):331-344. **3.** American Academy of Sleep Medicine. "International classification of sleep disorders." Diagnostic and coding manual (2005);51-55. **4.** ICD-10-CM tabular list of diseases and injuries. Centers for Medicare & Medicaid Services website. https://www.cms.gov/Medicare/Coding/ICD10/2020-ICD-10-CM. Accessed April 07, 2022. **5.** Dauvilliers Y, Evangelista E, Barateau L, et al. Measurement of symptoms in idiopathic hypersomnia: The Idiopathic Hypersomnia Severity Scale. Neurology. 2019;92(15):e1754-e1762. **6.** Trotti LM, Becker LA, Friederich Murray C, Hoque R. Medications for daytime sleepiness in individuals with idiopathic hypersomnia. *Cochrane Database Syst Rev.* 2021;5(5):CD012714.

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