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

IDIOPATHIC HYPERSOMNIA (IH)

EXPLORE THE EFFICACY & SAFETY OF XYWAV

The first and only FDA-approved treatment for your adult patients with IH.[1,2]

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.

IMPORTANT SAFETY INFORMATION

WARNING: CENTRAL NERVOUS SYSTEM DEPRESSION and ABUSE AND MISUSE.

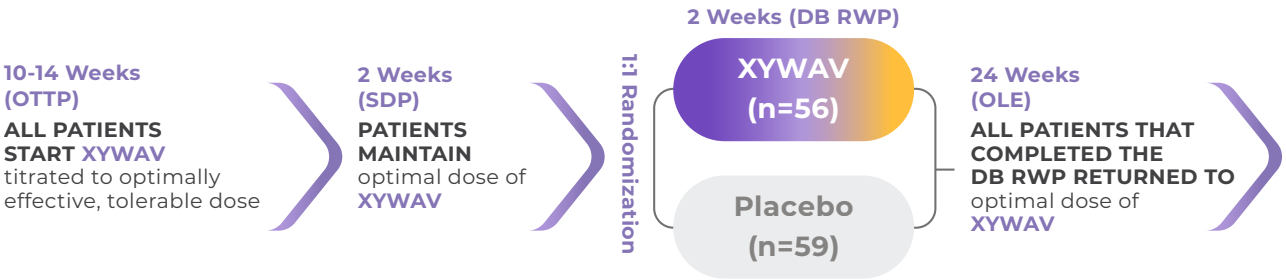
- **Central Nervous System Depression**
  XYWAV is a CNS depressant. Clinically significant respiratory depression and obtundation may occur in patients treated with XYWAV at recommended doses. Many patients who received XYWAV during clinical trials in idiopathic hypersomnia (IH) were receiving CNS stimulants.
- **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.

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

XYWAV: Evaluated in a large phase III study in a clinically relevant patient population with Idiopathic Hypersomnia (IH)[1,3-7]

Robust clinical trial	· Double-blind, placebo-controlled, randomized withdrawal, multicenter study of IH patients
Evaluated in adults	· 154 patients aged 19 to 75 (median age 39 years)
Over 6 months (204 days) mean exposure to XYWAV in safety population	· Included titration, stable-dose period, randomized withdrawal period, and open-label extension
Dosing regimens	· Participants took either a twice-nightly or a once-nightly regimen at the discretion of the clinician according to the clinical presentation of each patient · Approximately 57% of patients continued taking a stable dose of stimulant along with XYWAV throughout the SDP and DB RWP
Primary efficacy endpoint	· Change in Epworth Sleepiness Scale (ESS) score from the end of the stable-dose period to the end of the randomized withdrawal period
Key secondary endpoints (Change from end of SDP to end of DB RWP)	· Patient Global Impression of Change (PGIc) · Change in Idiopathic Hypersomnia Severity Scale (IHSS) score
Exploratory endpoint	· Mean change in Visual Analog Scale-Sleep Inertia (VAS-SI) daily scores from last week of SDP to the last week of DB RWP



DB RWP = Double-Blind, Randomized-Withdrawal Period; OLE = Open-Label Extension; OTTP = Open-Label Treatment Titration and Optimization Period; SDP = Stable-Dose Period.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

XYWAV was studied in an international, multicentered trial[7]

Treatment background (at baseline)[7]

Trial included patients (N=154) who were:

53%	Taking wake-promoting agents (WPA) or stimulants only
43%	Treatment naïve
3%	Taking sodium oxybate plus a WPA or stimulant
1%	Taking sodium oxybate only

Disease severity based on CGI-S (at baseline)[7]

Trial included patients (N=154) who were:

3%	Borderline to mildly ill
77%	Moderately to markedly ill
20%	Severely to extremely ill

Sleep time (at baseline)[7]

Trial included patients (N=154) who were:

20%	Patients with long sleep time (≥10 hours)
80%	Patients without long sleep time (<10 hours)

Long sleep time based on ICSD-II or ICSD-III criteria.[8]

The only FDA-approved treatment for IH: XYWAV was studied across multiple disease severities in Study 2.[1,2,7]

CGI-S = Clinical Global Impression of Severity; ICSD-III = International Classification of Sleep Disorders (3rd Edition)

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.

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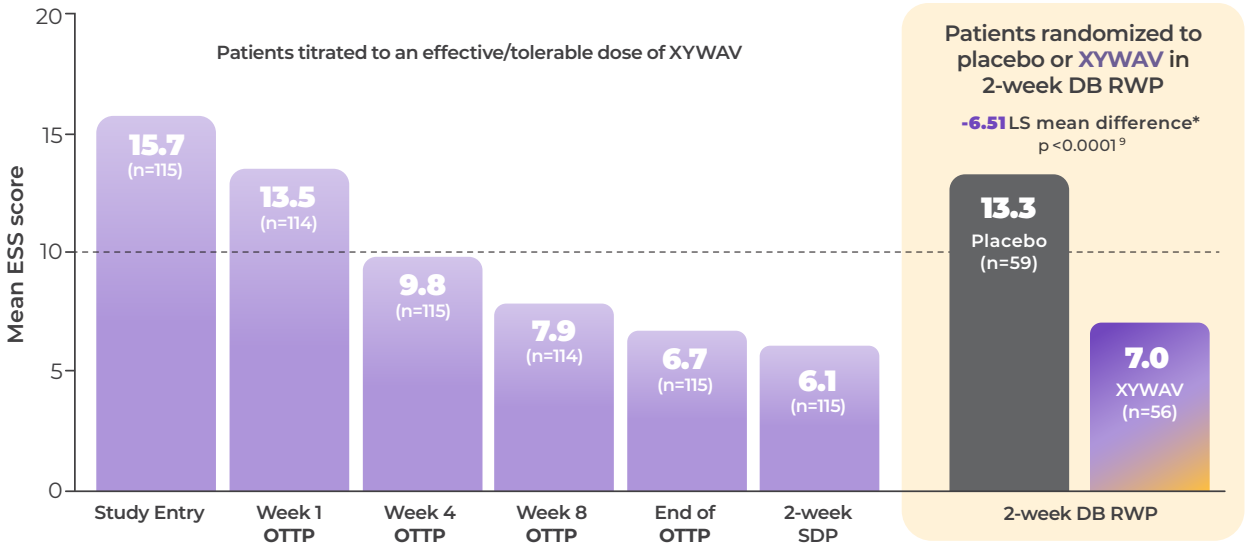
Primary efficacy endpoint: Efficacy in excessive daytime sleepiness (as measured by ESS)

Significant worsening of daytime sleepiness in patients randomized to placebo during the double-blind, randomized withdrawal period[1,9]

Mean ESS score remained stable from the end of the SDP through the end of the 2-week DB RWP with XYWAV—but worsened with placebo[1,9]



ESS scores higher than 10 are indicative of excessive daytime sleepiness.[10]

Limitations: Trial was not designed to demonstrate efficacy during the OTTP; all patients were taking active drug while dose was being titrated to individual optimized dose; no conclusions can be drawn about the effect of XYWAV during this period.

*LS mean difference between XYWAV and placebo in the change in ESS score from end of 2-week SDP to end of 2-week DB RWP[7]

IMPORTANT SAFETY INFORMATION (cont'd)

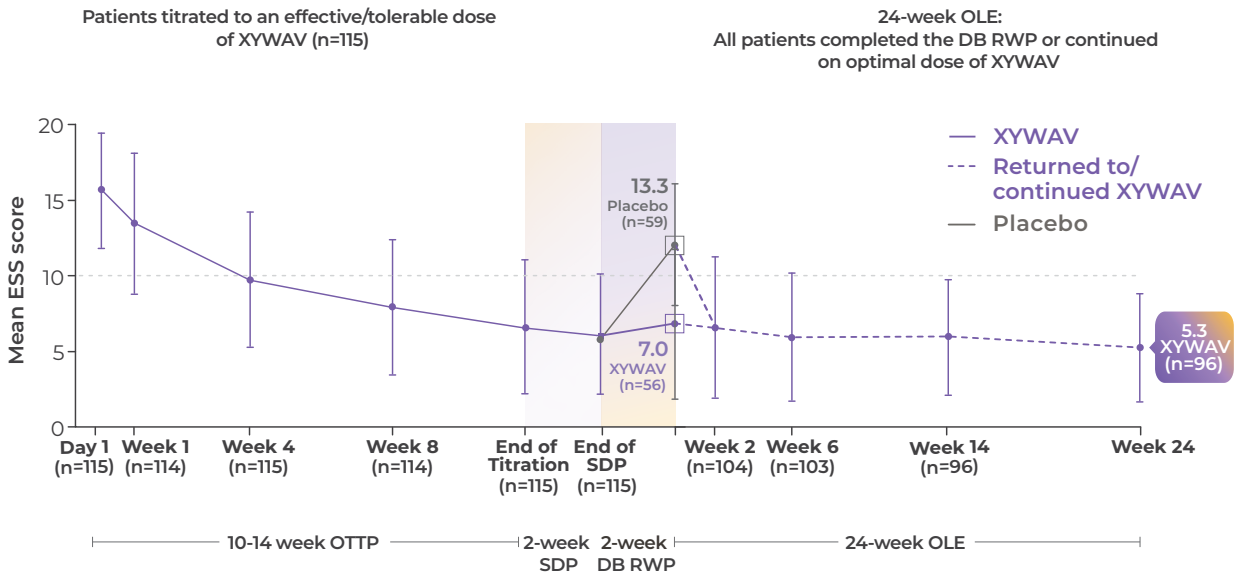
Warnings and Precautions (cont'd)

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.

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

Mean ESS score through the 24-week open-label extension period[9,11]



ESS scores higher than 10 are indicative of excessive daytime sleepiness.[10]

Limitations: Trial was only designed to evaluate efficacy during the DB RWP period. During the OTTP and OLE periods, all patients were taking active drug and no conclusions can be drawn about the effect of XYWAV. In addition, during the OLE, data are not available for all patients at all timepoints (number of patients declined over time).

94% of patients (106 out of 113) who completed the DB RWP (including those on placebo) continued into the XYWAV 24-week open label extension.[7]

DB RWP = Double-Blind, Randomized-Withdrawal Period; ESS = Epworth Sleepiness Scale; LS = Least Squares; OLE = Open-Label Extension; OTTP = Open-Label Treatment Titration and Optimization Period; SDP = Stable-Dose Period.

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.

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Key secondary endpoint: Patient perception of change in symptoms (as measured by PGIc)

Significantly more patients reported worsening* of IH overall when randomized to placebo during the double-blind, randomized withdrawal period[1]

Percentage of patients reporting worsening* idiopathic hypersomnia overall at the end of the 2-week DB RWP[1,11]

21%
reported worsening* in PGIc with XYWAV (n=56)

vs.

88%
reported worsening* in PGIc with placebo (n=59)

p<0.0001

79%

of patients continuing treatment with XYWAV reported improvement† or no change
in their overall IH at the end of DB RWP
(compared to how they felt during the stable-dose period)

*Worsening of idiopathic hypersomnia defined as "minimally, much, or very much worse" PGIc scores.[1]
†Improvement of IH defined as "minimally, much, or very much improved" PGIc scores.[11]
DB RWP = Double-Blind, Randomized-Withdrawal Period; PGIc = Patient Global Impression of Change.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

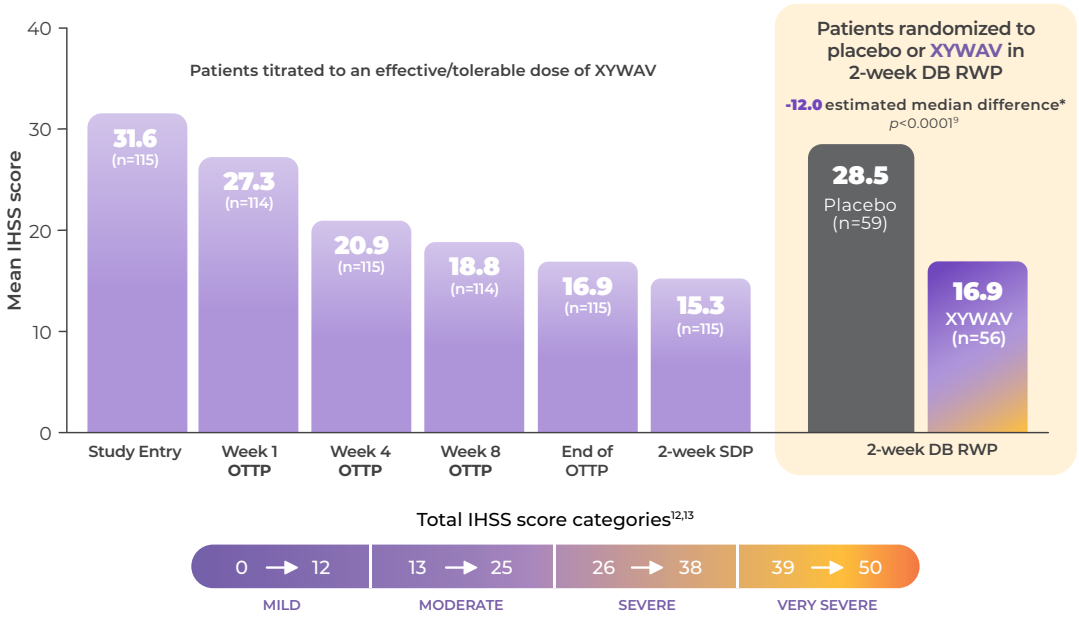
Respiratory Depression and Sleep-Disordered Breathing
XYWAV may impair respiratory drive, especially in patients with compromised respiratory function. In overdoses of oxybate and with illicit use of GHB, life-threatening respiratory depression has been reported. Increased apnea and reduced oxygenation 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 throughout and full Prescribing Information, including BOXED Warning.

Key secondary endpoint: Efficacy in IH symptom severity (as measured by IHSS)

Significant worsening of IH symptom severity in patients randomized to placebo during the double-blind, randomized withdrawal period[1,9]

Mean IHSS score remained stable from the end of the SDP through the end of the 2-week DB RWP with XYWAV—but worsened with placebo[1,9]



Limitations: Trial was not designed to demonstrate efficacy during the OTTP; all patients were taking active drug while dose was being titrated to individual optimized dose; no conclusions can be drawn about the effect of XYWAV during this period.

DB RWP = Double-Blind, Randomized-Withdrawal Period; IHSS = Idiopathic Hypersomnia Severity Scale; OTTP = Open-Label Treatment Titration and Optimization Period; SDP = Stable-Dose Period.

*Estimated median difference between XYWAV and placebo in change in IHSS from end of SDP to end of DB RWP[7]

XYWAV demonstrated efficacy vs placebo in mean IHSS score, which measures the severity and frequency of several key symptoms, including EDS, sleep inertia, cognitive impairment, and prolonged sleep time.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Depression and Suicidality

In Study 2, the pivotal 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.

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Exploratory endpoint

Visual Analog Scale for Sleep Inertia (VAS-SI)[6,7]

- A self-reported assessment tool to evaluate the intensity of a patient's sleep inertia
- Patients are presented with a single question:

How difficult was it for you to wake up this morning?

Very Easy **Very Difficult**

- They are then asked to mark their response on a 100-mm linear visual analog scale ranging from 0 (very easy) to 100 (very difficult)
- The patient's score is measured by taking the distance (mm) on the line between the "very easy" anchor and the patient's mark, providing a range of scores from 0–100

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Depression and Suicidality (cont'd)
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).

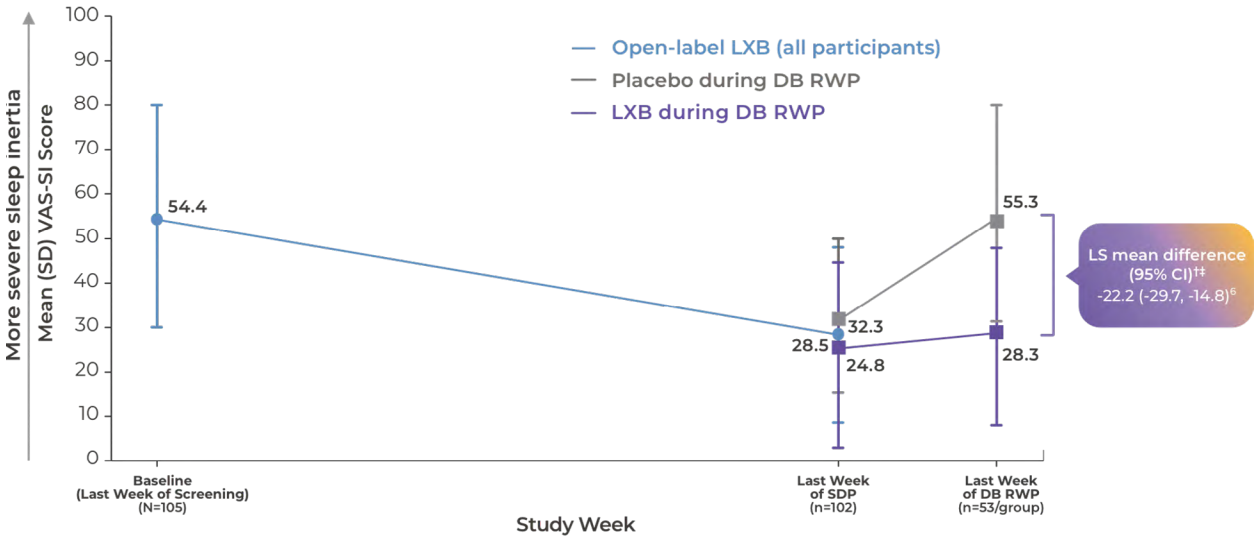
Episodes of sleepwalking should be fully evaluated and appropriate interventions considered.

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

Exploratory endpoint

Visual Analog Scale-Sleep Inertia (VAS-SI)[6,7]*

From the end of the SDP to the end of the DB RWP, mean VAS-SI scores changed from **32.3** to **55.3** in participants randomized to placebo, and from **24.8** to **28.3** for those who continued on XYWAV[6]



Limitations: This was an exploratory analysis and was outside of the statistical hierarchy; efficacy conclusions cannot be drawn. The LS mean difference and 95% CI were obtained from ANCOVA models. Covariates in the model included: baseline medication group, treatment group, and mean VAS-SI daily score at the last week of SDP.

CI = Confidence Interval; DB RWP = Double-Blind Randomized Withdrawal Period; LS = Least Squares; LXB = Lower-Sodium Oxybate; SD = Standard Deviation; SDP = Stable-Dose Period; VAS-SI = Visual Analog Scale for Sleep Inertia.

*Modified intent-to-treat population.
†Difference in change from end of SDP to end of DB RWP.
‡LXB, n=49; placebo, n=51.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Additional Adverse Reactions

Additional adverse reactions that occurred in ≥2% of adult patients with idiopathic hypersomnia treated with XYWAV in the Open-Label Titration and Stable Dose periods of Study 2 were balance disorder, muscle spasms, fall, paresthesia, snoring, weight decreased, bruxism, confusional state, depressed mood, feeling drunk, and irritability.

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Common adverse reactions[1]

Adverse reactions occurring in ≥2% of patients treated with XYWAV in the open-label titration and stable-dose periods[1]

Adverse reaction	Open-label titration period + stable-dose period, % (up to 16 weeks, N=154)
Nausea	21
Headache	16
Anxiety*	12
Dizziness	12
Insomnia†	9
Hyperhidrosis‡	8
Decreased appetite	8
Vomiting	7
Dry mouth	6
Diarrhea	5
Fatigue§	5
Somnolence‖	5
Tremor	5

Adverse reaction (cont'd)	Open-label titration period + stable-dose period, % (up to 16 weeks, N=154)
Parasomnia¶	5
Balance disorder#	3
Muscle spasms	3
Fall	3
Paresthesia	3
Snoring	3
Weight decreased	3
Bruxism	3
Confusional state	3
Depressed mood	3
Feeling drunk	3
Irritability	3

- The safety profile observed in Study 2 (IH Study) was similar to that of Study 1 (Narcolepsy Study)[1]

*Includes anxiety, nervousness, and panic attack.
†Includes middle insomnia, initial insomnia, insomnia, and terminal insomnia.
‡Includes hyperhidrosis and night sweats.
§Includes fatigue and asthenia.
‖Includes somnolence and sedation.
¶Includes confusional arousal, sleep paralysis, nightmare, sleep talking, somnambulism, and hypnopompic hallucination.
#Includes balance disorder and ataxia.

IMPORTANT SAFETY INFORMATION (cont'd)

Additional Adverse Reactions (cont'd)

Adverse reactions that occurred in ≥2% of patients in clinical studies with oxybate (but not in Study 2) and which may be relevant for XYWAV, were pain, pain in extremity, disturbance in attention, sleep paralysis, and disorientation.

Discontinuation: In Study 2, across all study periods (excluding placebo during the DB RWP) (up to 42 weeks), 17 of 154 (11%) patients withdrew from the trial due to adverse reactions, with anxiety the most common reason (3.2%). Other adverse reactions leading to study withdrawal included nausea, insomnia, vomiting, fatigue, feeling abnormal, fall, decreased appetite, dizziness, paresthesia, tremor, parasomnia, confusional state, hallucination visual, and irritability. The majority of adverse reactions leading to discontinuation began during the first few weeks of treatment.

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

Treatment doesn't have to wait until they've woken up in the morning[1]

XYWAV offers individualized twice- or once-nightly dosing so you can tailor optimal treatment for each of your patients with IH.[1]

	Twice-nightly dosing* Start at ≤4.5 g per night	Titrate to effect in increments of ≤1.5 g per night per week (divided into 2 doses)		
	EXAMPLE DOSING SCHEDULE			
Total Nightly Dosage	**4.5 g/night**	**6 g/night**	**7.5 g/night**	**9 g/night** (maximum total nightly dose)
Dose 1 (at bedtime)	**2.25 g**	**3 g**	**3.75 g**	**4.5 g**
Dose 2 (2.5-4 hours later)	**2.25 g**	**3 g**	**3.75 g**	**4.5 g**

Twice-nightly XYWAV—the dose for most: with 77% of IH patients concluding the DB RWP of the clinical trial on this dosing regimen[1,14]

*For twice-nightly regimens, doses can be divided equally or unequally. Some patients may achieve better responses with unequal doses at bedtime and 2.5 to 4 hours later.[1]

	Once-nightly dosing Start at ≤3 g per night	Titrate to effect in increments of ≤1.5 g per night per week	
	EXAMPLE DOSING SCHEDULE		
Total Nightly Dosage	**3 g/night** (total)	**4.5 g/night** (total)	**6 g/night** (maximum total nightly dose)

In the clinical trial, participants took XYWAV alone or with wake-promoting agents and/or stimulants based on their treatment regimen at enrollment.[1,7] During titration, the dosing regimen may be changed as needed based on efficacy and tolerability.[1] Be sure to follow-up with your XYWAV patients so they get an optimally tailored dose.

- For either dosing regimen, patients should take the first nightly dose of XYWAV at bedtime at least 2 hours after eating[1]
- The increase in the total nightly dose should NOT exceed 1.5 g per week[1]
- Total doses >9 g per night or single doses >6 g per night have not been studied and ordinarily should not be administered[1]
- In the clinical study, when patients were switched from twice- to once-nightly dosing, the total nightly dose was initially the same as the first dose of the twice-nightly dosing regimen.[1] When patients were switched from once- to twice-nightly dosing, the total combined twice-nightly dose was no more than 1.5 g higher than the single dose.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Drug Interactions

XYWAV is contraindicated in combination with alcohol or sedative hypnotics. Use of other CNS depressants may potentiate the CNS-depressant effects of XYWAV.

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The XYWAV and XYREM REMS: Managing known or potential serious risks

- **XYWAV is available only through a restricted distribution program called the XYWAV and XYREM REMS** because of the risks of central nervous system depression and abuse and misuse
- 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 Certified Pharmacy

XYWAV will be dispensed and shipped only to patients who are enrolled in the XYWAV and XYREM REMS with documentation of safe use

Learn more or register at **XYWAVXYREMREMS.com** or call 1-866-997-3688.

REMS = Risk Evaluation and Mitigation Strategy.

IMPORTANT SAFETY INFORMATION (cont'd)

Drug Interactions (cont'd)

Concomitant use of sodium oxybate with divalproex sodium results in an increase in systemic exposure to GHB, which was shown to cause a greater impairment on some tests of attention and working memory in a clinical study. A similar increase in exposure is expected with concomitant use of XYWAV and divalproex sodium; therefore, an initial dose reduction of XYWAV is recommended when used concomitantly with divalproex sodium. Prescribers are advised to monitor patient response closely and adjust dose accordingly if concomitant use of XYWAV and divalproex sodium is warranted.

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

JazzCares® for XYWAV is your partner in supporting your patients throughout their treatment journey

Jazz Cares®
Making a difference in Patients' lives, one Patient at a time

Our program is designed to support your patients' needs from day 1

Prior authorization and reimbursement support*†

Our JazzCares® reimbursement experts will not only get you the coverage details you're looking for, but they can also help with the prior authorization process, so you can better focus on your patients.

For XYWAV: Over 75% of cases submitted through CoverMyMeds receive an outcome in less than 4 hours!*

Nurse and pharmacy support

Our dedicated Nurse Case Managers can help your patients navigate social support, address practical challenges, get them motivated, and elevate their confidence, all according to their unique needs.

A pharmacist is also available 24/7 through phone or video chat.

Personalized resources

Give your patients the support they need to reach their goals through personalized emails and texts based on their unique needs.

Encourage your patients to sign up for the myWAV™ app.

Patients who have commercial insurance coverage may pay as little as $5 per prescription.‡

*Insurance coverage and plans may vary. The JazzCares program at Jazz Pharmaceuticals provides general information only and is not a guarantee of any coverage or reimbursement outcome. All treatment decisions rest solely with the treating physician or qualified healthcare professional.

†See Terms and Conditions for eligibility.

‡Subject to a maximum annual benefit.

IMPORTANT SAFETY INFORMATION (cont'd)

Pregnancy and Lactation

There are no adequate data on the developmental risk associated with the use of XYWAV or sodium oxybate in pregnant women. XYWAV should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. GHB is excreted in human milk after oral administration of sodium oxybate.

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IMPORTANT SAFETY INFORMATION (cont'd)

Pregnancy and Lactation (cont'd)

There is insufficient information on the risk to a breastfed infant, and there is insufficient information on milk production in nursing mothers. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for XYWAV and any potential adverse effects on the breastfed infant from XYWAV or from the underlying maternal condition.

Pediatric Use

Safety and effectiveness of XYWAV for the treatment of idiopathic hypersomnia in pediatric patients have not been established.

Geriatric Use

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Hepatic Impairment

The starting dose of XYWAV should be reduced in patients with liver impairment.

Dosage Modification in Patients with Hepatic Impairment: The recommended starting dosage in patients with hepatic impairment is one-half of the original dosage per night, administered orally, divided into two doses.

Dependence and Tolerance

There have been case reports of withdrawal, ranging from mild to severe, following discontinuation of illicit use of GHB at frequent repeated doses (18 g to 250 g per day) in excess of the recommended dosage range. Signs and symptoms of GHB withdrawal following abrupt discontinuation included insomnia, restlessness, anxiety, psychosis, lethargy, nausea, tremor, sweating, muscle cramps, tachycardia, headache, dizziness, rebound fatigue and sleepiness, confusion, and, particularly in the case of severe withdrawal, visual hallucinations, agitation, and delirium. These symptoms generally abated in 3 to 14 days. In cases of severe withdrawal, hospitalization may be required.

In the XYWAV clinical trial in adult idiopathic hypersomnia patients at recommended doses, six patients reported insomnia, two patients reported early insomnia, and one patient reported visual and auditory hallucinations following abrupt discontinuation of XYWAV.

Tolerance to XYWAV has not been systematically studied in controlled clinical trials. There have been some case reports of symptoms of tolerance developing after illicit use at dosages far in excess of the recommended XYWAV dosage regimen.

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.** FDA grants first of its kind indication for chronic sleep disorder treatment. News release. U.S. Food and Drug Administration; August 12, 2021. Accessed March 18, 2024. https://www.fda.gov/news-events/press-announcements/fda-grants-first-its-kind-indication-chronic-sleep-disorder-treatment **3.** A multicenter study of the efficacy and safety of JZP-258 in the treatment of idiopathic hypersomnia (IH) with an open-label safety extension. ClinicalTrials.gov identifier: NCT03533114. Updated June 11, 2021. Accessed March 18, 2024. https://clinicaltrials.gov/ct2/show/NCT03533114 **4.** U.S. National Library of Medicine. Clinicaltrials.gov search results for Idiopathic Hypersomnia. Updated June 11, 2021. Accessed March 10, 2024. https://clinicaltrials.gov/ct2/results?cond=Idiopathic+Hypersomnia **5.** Sodium oxybate in idiopathic hypersomnia (SODHI). ClinicalTrials.gov identifier: NCT03597555. Updated February 12, 2021. Accessed March 18, 2024. https://clinicaltrials.gov/ct2/show/NCT03597555 **6.** Bogan K, Dauvilliers Y, Thorpy MJ et al. Effect of lower-sodium oxybate on sleep inertia in idiopathic hypersomnia in a double-blind randomized withdrawal study. Poster presented at: Sleep 2021, the 35th Annual Meeting of the Associated Professional Sleep Societies (APSS); June 10-13, 2021; Virtual Meeting. **7.** Dauvilliers Y, Arnulf I, Foldvary- Schaefer N, et al. Safety and efficacy of lower-sodium oxybate in adults with idiopathic hypersomnia: a phase 3, placebo-controlled, double-blind, randomised withdrawal study. *Lancet Neurol.* 2022;21(1):53-65. **8.** American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014. **9.** Data on File (XYW-2021-040). Palo Alto, CA: Jazz Pharmaceuticals, Inc. **10.** Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep.* 1991;14(6):540- 545. **11.** Dauvilliers Y, Arnulf I, Foldvary-Schaefer N, et al. Placebo-controlled, double-blind, randomized withdrawal study of lower-sodium oxybate in adults with idiopathic hypersomnia. Poster presented at: Sleep 2021, the 35th Annual Meeting of the Associated Professional Sleep Societies (APSS); June 10-13, 2021; Virtual Meeting. **12.** 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. **13.** Rassu AL, Evangelista E, Barateau L, et al. Idiopathic Hypersomnia Severity Scale to better quantify symptoms severity and their consequences in idiopathic hypersomnia. *J Clin Sleep Med*. 2022;18(2):617-629. **14.** Data on File (JZP080-301-20). Palo Alto, CA: Jazz Pharmaceuticals, Inc. **15.** Takenoshita S, Nishino S. Pharmacologic management of excessive daytime sleepiness. *Sleep Med Clin*. 2017;12(3):461-478. **16.** Boulos MI, Murray BJ. Current evaluation and management of excessive daytime sleepiness. *Can J Neurol Sci.* 2010;37(2):167-176.

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

Why choose XYWAV?

XYWAV is the only FDA-approved treatment for idiopathic hypersomnia (IH) in adults[1,2]

HELP PREPARE YOUR PATIENTS WITH IH FOR MULTIPLE DAILY SYMPTOMS[1,15,16]

Unlike stimulants and wake-promoting agents that are taken during the day, XYWAV is taken each night to help manage multiple daily symptoms of IH, including:

- Excessive daytime sleepiness (EDS)
- Sleep inertia
- Cognitive impairment
- Prolonged sleep time

DEMONSTRATED EFFICACY & AN ESTABLISHED SAFETY PROFILE[1,7]

XYWAV efficacy and safety was evaluated in a phase III, double-blind, placebo-controlled, randomized withdrawal, multicenter study of 154 adult patients with IH aged 19 to 75

- Statistically significant differences in ESS score, PGIc, and IHSS score with XYWAV vs placebo from end of SDP to end of DB RWP
- Of 113 patients who completed the DB RWP (including those on placebo), 106 continued into the XYWAV 24-week open label extension

The safety profile observed in Study 2 (IH Study) was similar to that of Study 1 (Narcolepsy Study).

TREATMENT DOESN'T HAVE TO WAIT UNTIL THEY'VE WOKEN UP IN THE MORNING[1]

XYWAV offers individualized twice- or once-nightly dosing, so you can tailor treatment to each of your patients with IH.

JazzCares® for XYWAV, your partner in support

JazzCares® for XYWAV is committed to getting your patients the support and resources throughout treatment—from access and affordability assistance, to nurse case managers and more.

DB RWP = Double-Blind, Randomized-Withdrawal Period; ESS = Epworth Sleepiness Scale; FDA = Food and Drug Administration; IHSS = Idiopathic Hypersomnia Severity Scale; PGIc = Patient Global Impression of Change.

IMPORTANT SAFETY INFORMATION

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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Jazz Pharmaceuticals