Jazz Pharmaceuticals Showcases Phase 4 Data Demonstrating Xywav® (calcium, magnesium, potassium, and sodium oxybates) Oral Solution Treatment Effects and Real-World Evidence at World Sleep and Psych Congresses

September 22, 2025

20 abstracts presented across World Sleep and Psych Congresses showcase Jazz's leadership in sleep medicine

Novel results from the Phase 4 DUET trial underscore the significance of appropriate treatment options in adults with narcolepsy or idiopathic hypersomnia

For U.S. media and investors only

DUBLIN, Sept. 22, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced new real-world evidence and Phase 4 data reinforcing the value of Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution treatment outcomes in adults with narcolepsy or idiopathic hypersomnia (IH) were presented at World Sleep 2025, held in Singapore from September 5-10, 2025, as well as the 38th annual Psych Congress, held in San Diego from September 17-21, 2025. Notable Phase 4 data included new results from the DUET (Develop hypersomnia Understanding by Evaluating low-sodium oxybate Treatment) trial, showing treatment effects of low-sodium *Xywav* on daytime and nighttime symptoms of narcolepsy or IH. The DUET trial is a Phase 4, prospective, single-arm, open-label study to assess the effect of *Xywav* treatment on excessive daytime sleepiness, polysomnography parameters, and functional outcomes in adults with narcolepsy or IH.

"These new DUET data presented by Jazz continue to show the importance of measuring and understanding the impact of treatment in both daytime and nighttime symptoms, as well as other functional outcomes in people living with narcolepsy or idiopathic hypersomnia," said Logan Schneider, MD, adjunct clinical associate professor of sleep medicine, Stanford Sleep Center and Consultant Neurologist, Standford/VA Alzheimer's Center. "These results further reflect the positive implications that an appropriate treatment can have on patients' sleep outcomes, holistic health and their daily functioning."

"We are leveraging both the power of Phase 4 clinical trials and real-world evidence to provide clinically meaningful, high-quality research for the global sleep community, which informs the health complexities of people living with narcolepsy and idiopathic hypersomnia," said Kelvin Tan, MB BCh, MRCPCH, chief medical affairs officer of Jazz Pharmaceuticals. "These robust data continue to expand our understanding of sleep disorders and the challenges patients living with these conditions face while further reinforcing the value of low-sodium *Xywav* treatment."

Presentation highlights include:

- ***Xywav* DUET Sleep Actigraphy Results (World Sleep Poster #97):** Novel analysis of DUET data examining the impact of *Xywav* treatment on actigraphy measures found participants with narcolepsy experienced fewer awakenings and decreased wake after sleep onset, suggesting improved sleep measures. Similarly, participants with IH treated with *Xywav* experienced fewer awakenings, suggesting improved sleep measures, as well as decreased nocturnal sleep time.
- ***Xywav* DUET Sleep Inertia and Components of Daytime Sleepiness Results (World Sleep Poster #92):** Analysis of DUET data evaluating Psychomotor Vigilance Test (PVT) lapses and Karolinska Sleepiness Scale (KSS) ratings among participants with IH receiving optimized *Xywav* treatment, demonstrated reduced sleep inertia magnitude by subjective and objective measures, subjective reduction in sleepiness upon waking and objective improvement in impaired alertness.
- **Real-World Risk of Sodium-Associated Negative Clinical Outcomes Results (World Sleep Poster #101 and #186):** Real-world analysis assessing the risk of sodium-associated negative clinical outcomes (NCOs) showed individuals with narcolepsy or IH have an elevated risk of development or progression of cardiovascular, cardiometabolic and renal NCOs relative to those without these conditions. These results emphasized the need to reduce sodium intake to mitigate the risk of NCOs among those living with these conditions.
- ***Xywav* DUET >9 Gram Cohort (Psych Congress Poster #125):** Complete cohort (n=48) analysis of top-line efficacy and safety data from DUET trial participants with narcolepsy taking 9-12 grams of *Xywav* nightly experienced additional symptom benefits, with reductions in Epworth Sleepiness Scale, Narcolepsy Severity Scale scores and cataplexy attacks, as compared to taking 9 grams per night at baseline. The *Xywav* label recommends a nightly dose of 6-9 grams per night for adults with narcolepsy. Overall, treatment-emergent adverse events were consistent with the known safety profile of *Xywav* at dosages less than 9 grams per night.

The abstracts presented at World Sleep 2025 are available online at ws2025.abstractserver.com/program.

The Psych Congress presentations are available on-demand through the conference mobile application. Abstracts and posters will also be published on HMP Global's Psychiatry & Behavioral Health Learning Network 30-60 days after the congress ends.

Presentation Title	Lead Author	Presentation Details
World Sleep Congress		

Risk of New-onset Cardiovascular and Cardiometabolic Conditions in Narcolepsy: An Analysis of the *All of Us* Research Program	SC Markt	Poster #: 212 Presenter: SC Markt
Real-world Risk of Sodium-Associated Negative Clinical Outcomes Among Individuals With Narcolepsy in the United States	SC Markt	Poster #: 186 Presenter: SC Markt
Risk of Sodium-Associated Negative Clinical Outcomes in Individuals With Idiopathic Hypersomnia in the United States: A Real-world Analysis	SC Markt	Poster #: 101 Presenter: SC Markt
Association Between Sodium Intake and Systolic and Diastolic Blood Pressure: A Systematic Literature Review and Meta-analysis	C Drachenberg	Poster #: 237 Presenter: C Drachenberg
Association Between Sodium Intake and Risk of Hypertension, Heart Failure, Stroke, and Myocardial Infarction: A Systematic Literature Review and Meta-analysis	C Drachenberg	Poster #: 211 Presenter: J Sacks
Prevalence and Incidence of Comorbidities in individuals With Narcolepsy or Idiopathic Hypersomnia: A Systematic Literature Review	C Drachenberg	Poster #: 193 Presenter: C Drachenberg
Estimating the Economic and Clinical Effects of High- and Low-Sodium Oxybate Agents among the US Population with Narcolepsy: Microsimulation Cost Analysis	L Pinto	Poster #: 177 Presenter: C Drachenberg
Sleep Architecture With Low-Sodium Oxybate Treatment in Narcolepsy: Results From the DUET Study	CM Ruoff	Poster #: 184 Presenter: DA Nichols
Sleep Architecture With Low-sodium Oxybate Treatment In Idiopathic Hypersomnia: Results From The DUET Study	A Cairns	Poster #: 120 Presenter: DA Nichols
Sleep Actigraphy in Participants With Narcolepsy or Idiopathic Hypersomnia Taking Low-Sodium Oxybate: Results From the DUET Study	N Foldvary-Schaefer	Poster #: 097 Presenter: JK Alexander
Reduction in Sleep Inertia and Components of Daytime Sleepiness in Idiopathic Hypersomnia With Low-Sodium Oxybate Treatment in the Phase 4 DUET Study	H Van Dongen	Poster #: 092 Presenter: H Van Dongen
Impact of Switching From High- to Low-Sodium Oxybate on Ambulatory Blood Pressure in People With Narcolepsy	Y Dauvilliers	Poster #: 216 Presenter: Y Dauvilliers
Psych Congress		
Effectiveness and Safety of Low-Sodium Oxybate in Participants With Idiopathic Hypersomnia With or Without Psychiatric Comorbidities: Results From the Phase 4	DT Plante	Poster #: 123 Presenter: DT Plante

DUET Study		
Improvement in Bothersome Mood, Cognitive, and Functional Impacts of Idiopathic Hypersomnia After Low-Sodium Oxybate Treatment in the DUET Study	DT Plante	Poster #: 124 Presenter: DT Plante
Impact of Sleep Inertia on Cognition in People With Idiopathic Hypersomnia	SC Markt	Poster #: 128 Presenter: AT Togun
Evaluating the Impact of Switching From High-Sodium Oxybate to Low-Sodium Oxybate on Ambulatory Blood Pressure in People With Narcolepsy	VK Somers	Poster #: 129 Presenter: DA Nichols
Greater Than 9 Gram Dosage of Low-Sodium Oxybate in Study Participants With Narcolepsy: Effectiveness and Safety Results From the DUET Study	JK Simmons	Poster #: 125 Presenter: JK Alexander
Effectiveness and Safety of Low-Sodium Oxybate in Participants With Narcolepsy With or Without Psychiatric Comorbidities: Results From the Phase 4 DUET Study	CM Ruoff	Poster #: 120 Presenter: DA Nichols
Self-Reported Cognitive Complaints and Work Productivity in Participants With Narcolepsy After Low-Sodium Oxybate Treatment: Results From the Phase 4 DUET Study	LD Schneider	Poster #: 126 Presenter: JK Alexander
Clinical Characteristics and Productivity Losses Among Individuals Diagnosed With Narcolepsy or Idiopathic Hypersomnia	AT Togun	Poster #: 113 Presenter: AT Togun

About Narcolepsy

Narcolepsy is a chronic, debilitating neurologic sleep disorder characterized by the inability to maintain continuous sleep at night and sustained wakefulness throughout the day. This leads to symptoms that can include fragmented or disrupted nighttime sleep, excessive daytime sleepiness, and cataplexy.[1] Patients with EDS due to narcolepsy experience sleep attacks and, despite fighting the urge to sleep, may unintentionally fall asleep for short periods.[2,3] These sleep attacks may happen at inappropriate or potentially dangerous times such as during driving, cycling, eating, or mid-conversation.[4]

There is no cure for narcolepsy; the symptoms are lifelong and have a substantial negative impact on a person's ability to function psychologically, socially and professionally.[5] Patients with narcolepsy are at increased risk for hypertension, cardiometabolic morbidity, stroke, myocardial infarction, heart failure, cardiac arrest, and death.[6,7,8,9] As narcolepsy is a chronic condition that requires lifelong treatment, early access to an effective treatment can help reduce the impact of narcolepsy symptoms on a person's physical and mental health, and long-term impacts of the treatment on cardiovascular health should be considered.[5]

About Idiopathic Hypersomnia

Idiopathic hypersomnia is an often debilitating, neurologic sleep disorder that goes beyond chronic excessive daytime sleepiness.[10,11,12,13] Idiopathic hypersomnia is a 24-hour sleep disorder, and symptoms may include non-restorative sleep with or without long sleep time (main, nighttime, sleep episode of more than 9 hours, or a sleep duration of 11 hours or longer over a 24-hour period); severe sleep inertia (prolonged difficulty waking, with frequent reentries into sleep, confusion, and irritability); long and unrefreshing naps; cognitive impairment and brain fog, or the inability to focus for long periods of time.[10,11,12,13,14] Although there are some overlapping clinical features with narcolepsy, idiopathic hypersomnia is a condition with its own specific diagnostic criteria.[13,15]

Idiopathic hypersomnia is an often debilitating illness that can significantly affect social, educational, and occupational functioning.[16,17] In the U.S., approximately 37,000 adult patients have been diagnosed with idiopathic hypersomnia and are actively seeking healthcare.[18] This low number of people may be due to the many difficulties in identifying and diagnosing idiopathic hypersomnia, as well as distinguishing it from other similar sleep disorders. It is estimated that far fewer patients are currently receiving pharmacological treatment for their idiopathic hypersomnia.[18,19,20,21]

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

Xywav is the only low-sodium oxybate approved by the U.S. Food and Drug Administration (FDA) for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. The FDA recognized seven years of Orphan Drug Exclusivity for *Xywav* for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy. The Office of Orphan Product Development (OOPD) at the FDA

also published its summary of clinical superiority findings for *Xywav* for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy by means of greater cardiovascular safety compared to Xyrem® (sodium oxybate) oral solution. The decision of the OOPD is based on the FDA findings that *Xywav* provides a greatly reduced chronic sodium burden compared to *Xyrem*. *Xywav* has 131 mg of sodium at the maximum recommended nightly dose whereas other high sodium oxybates have 1640 mg at the equivalent dose. *Xywav* is comprised of a unique composition of cations resulting in 92% less sodium, or a reduction of approximately 1,000 to 1,500 mg/night at the recommended dose range of 6 g to 9 g/night. *Xywav* is the only oxybate therapy that does not carry a warning in the label related to use in patients sensitive to high sodium intake.

Xywav is also the first and only U.S. FDA-approved treatment option for idiopathic hypersomnia in adults. The FDA recognized seven years of Orphan Drug Exclusivity for *Xywav* for the treatment of idiopathic hypersomnia in adults. *Xywav* is the only FDA-approved treatment studied across the multiple symptoms of idiopathic hypersomnia, such as EDS, sleep inertia (severe grogginess or confusion when waking up), long sleep duration and cognitive impairment. *Xywav* can be administered as a twice- or once-nightly regimen for the treatment of idiopathic hypersomnia in adults.

The exact mechanism of action of *Xywav* in the treatment of adults with idiopathic hypersomnia and of cataplexy and EDS in narcolepsy is unknown. It is hypothesized that the therapeutic effects of *Xywav* are mediated through $GABA_B$ actions during sleep at noradrenergic and dopaminergic neurons, as well as thalamocortical neurons.[22] The U.S. Drug Enforcement Agency (DEA) has designated *Xywav* as a Schedule III medicine. The DEA defines Schedule III drugs, substances, or chemicals as drugs with a moderate to low potential for physical and psychological dependence.[22,23] Because of the risks of central nervous system (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.

Important Safety Information for Xywav

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.

Contraindications
XYWAV is contraindicated

- in combination with sedative hypnotics or alcohol and
- in patients with succinic semialdehyde dehydrogenase deficiency.

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 (e.g., 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 (e.g., 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.

Abuse and Misuse
XYWAV is a Schedule Ill 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 (e.g., assault victim). Physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely.

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 1, the randomized-withdrawal clinical trial in adult patients with narcolepsy (n=201), depression and depressed mood were reported in 3% and 4%, respectively, of patients treated with XYWAV. Two patients (1%) discontinued XYWAV because of depression. In most cases, no change in XYWAV treatment was required.

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 1, confusion and anxiety occurred in 1% and 5% of patients with narcolepsy treated with XYWAV, respectively. One patient experienced visual hallucinations and confusion after ingesting approximately 9 grams of XYWAV.

In Study 2, confusion and anxiety occurred in 3% and 16% of patients with idiopathic hypersomnia, respectively. One patient 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 1 and Study 2, parasomnias, including sleepwalking, were reported in 6% and 5% of adult patients treated with XYWAV, respectively.

In a clinical trial of XYREM (same active moiety as XYWAV) in adult patients with narcolepsy, five instances of sleepwalking with potential injury or significant injury were reported. Parasomnias, including sleepwalking, 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) that included pediatric patients 7 to 17 years of age 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 overall adverse reaction profile of XYREM in the pediatric clinical trial was similar to that seen in the adult clinical trial program. 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.

Additional Adverse Reactions
Adverse reactions that occurred in 2-<5% of adult patients treated with XYWAV in the Open Label Titration and Stable Dose Periods of the randomized-withdrawal study in adult patients with narcolepsy with cataplexy (Study 1) were fatigue, dry mouth, depressed mood, enuresis, irritability, paresthesia, depression, tremor, somnolence, and muscle spasms. Adverse reactions occurring in 2-<5% of patients treated with XYWAV in the IH study include balance disorder, muscle spasms, fall, paresthesia, snoring, weight decreased, bruxism, confusional state, depressed mood, feeling drunk, and irritability.

Adverse reactions that occurred in ≥2% of patients in clinical studies with oxybate (but not in Study 1) and which may be relevant for XYWAV, were pain, feeling drunk, pain in extremity, cataplexy, disturbance in attention, sleep paralysis, and disorientation.

Discontinuation: In Study 1, 9 of 201 patients (4%) reported adverse reactions that led to withdrawal from the study (anxiety, decreased appetite, depressed mood, depression, fatigue, headache, irritability, nausea, pain in extremity, parasomnia, somnolence, and vomiting). The most common adverse reaction leading to discontinuation was nausea (1.5%). In Study 2, 17 of 154 (11%) patients across all study periods (excluding placebo during the DB RWP) (up to 42 weeks) reported adverse reactions that led to withdrawal from the study (anxiety, nausea, insomnia, vomiting, fatigue, feeling abnormal, fall, decreased appetite, dizziness, paresthesia, tremor, parasomnia, confusional state, hallucination visual, and irritability). The most common adverse reaction leading to discontinuation was anxiety (3.2%). In Study 1 and Study 2, the majority of adverse reactions leading to discontinuation began during the first few weeks of treatment.

In the pediatric clinical trial with XYREM (same active moiety as XYWAV), 7 of 104 patients reported adverse reactions that led to withdrawal from the study (hallucination, tactile; suicidal ideation; weight decreased; sleep apnea syndrome; affect lability; anger, anxiety, depression; and headache).

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.

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.

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. 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
The safety and effectiveness of XYWAV for the treatment of cataplexy or excessive daytime sleepiness in pediatric patients 7 years of age and older with narcolepsy have been established. XYWAV has not been studied in a pediatric clinical trial for narcolepsy or IH. Use of XYWAV in pediatric patients 7 years of age and older with narcolepsy is supported by evidence from an adequate and well-controlled study of sodium oxybate in pediatric patients 7 to 17 years of age, a study in adults showing a treatment effect of XYWAV similar to that observed with sodium oxybate, pharmacokinetic data of sodium oxybate from adult and pediatric patients, and pharmacokinetic data of XYWAV from healthy adult volunteers.

Safety and effectiveness of XYWAV in pediatric patients below the age of 7 years with narcolepsy have not been established.

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 clinical trial experience with XYREM in narcolepsy/cataplexy patients at recommended doses, two patients reported anxiety and one reported insomnia following abrupt discontinuation at the termination of the clinical trial; in the two patients with anxiety, the frequency of cataplexy had increased markedly at the same time. In the XYWAV clinical trial in adult narcolepsy/cataplexy patients at recommended doses, one patient reported insomnia following abrupt discontinuation of XYWAV. 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 full Prescribing Information, including BOXED Warning here: https://pp.jazzpharma.com/pi/xywav.en.USPI.pdf

About Jazz Pharmaceuticals
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharma company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing potentially life-changing medicines for people with serious diseases — often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience. Jazz is headquartered in Dublin, Ireland with research and development laboratories, manufacturing facilities and employees in multiple countries committed to serving patients worldwide. Please visit www.jazzpharmaceuticals.com for more information.

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