



Jazz Pharmaceuticals to Present Latest Advancements in Sleep Medicine at World Sleep 2023

October 18, 2023

Meeting presentations underscore the increased need for awareness around the cardiovascular and cardiometabolic comorbidities and modifiable risk factors associated with sleep disorders

Fourteen abstracts demonstrate Jazz Pharmaceuticals' continued leadership and commitment to expanding knowledge across rare sleep disorders

DUBLIN, Oct. 18, 2023 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the Company and its partners will present 14 abstracts from across its sleep medicine portfolio, including two oral presentations, at the 17th annual World Sleep 2023 Congress, held October 20-25 in Rio de Janeiro, Brazil.

The oral presentations include findings from the real-world TENOR study, which demonstrated individualized dosing strategies for twice-nightly oxybate treatment in narcolepsy. In addition, findings from the CV-RHYTHM study will be presented at the meeting, which found that patients with idiopathic hypersomnia experienced a significantly higher prevalence of cardiovascular comorbidities, including stroke, heart attacks and heart failure than those without this underrecognized sleep disorder.

"Findings from the CV-RHYTHM study emphasize the importance of a holistic management plan and play an important role in providing insights to clinicians on how to approach treating sleep disorders, like idiopathic hypersomnia," said Logan Schneider, MD, clinical assistant professor (affiliated) of sleep medicine, Stanford Sleep Center and Consultant Neurologist, Stanford/VA Alzheimer's Center. "Based on administrative claims data and consistent with observational studies in patients diagnosed with narcolepsy, the study found that compared to patients without idiopathic hypersomnia, patients with the condition are more likely to experience cardiovascular comorbidities, including cardiovascular disease, stroke, heart attacks and heart failure."

Highlights at World Sleep 2023 include:

- An exploratory, post-hoc analysis from two Phase 3 trials of low-sodium Xywav[®] (calcium, magnesium, potassium, and sodium oxybates) oral solution in narcolepsy and idiopathic hypersomnia that examined changes in blood pressure among patients previously naïve to oxybate therapy, finding that there were no clinically meaningful differences from baseline in systolic blood pressure in those treated with Xywav during the open-label study periods.
- A systematic review of literature evaluating the relationship between sodium intake and clinical outcomes that demonstrated statistically significant associations between sodium intake and cardiovascular and cardiometabolic outcomes, as well as cardiorenal conditions and certain cancers.
- An analysis of patient preferences and experiences during transition from high-sodium Xyrem[®] (sodium oxybate) oral solution to low-sodium Xywav in adult narcolepsy patients from the real-world TENOR study and interventional SEGUE study, where most patients reported that the switch was easy, with minimal modifications to their dosing regimen, and that they preferred Xywav over Xyrem, primarily due to its lower sodium content.

"These presentations continue to build on our body of research demonstrating the clear relationship between sleep disorders and increased cardiovascular risk, as well as the meaningful improvements possible with treatment plans that consider a patient's holistic health, such as reducing sodium intake," said Rob Iannone, MD, MSCE, executive vice president and global head of research and development of Jazz Pharmaceuticals. "We have a deep commitment to expanding our understanding of sleep disorders so that we can better support patients living with limited treatment options. The findings from these studies inform our growing R&D pipeline which we hope will deliver the next generation of transformative medicines to patients in need."

The World Sleep 2023 schedule is [available online](#) and outlines all abstracts, posters and oral presentations slated to be shared at the congress. All abstracts are published in a supplemental issue of *Sleep Medicine*, the official journal of World Sleep Society, two months after the event.

A full list of Jazz Pharmaceuticals' presentations follows below:

| Presentation Title | Lead Author | Session Number & Title / Date & Time (BRT) / Presentation Number |
|--|-------------|---|
| Oral Presentations | | |
| Individualized Dosing Strategies for Oxybate: Insights From the Real-World TENOR Study | W Macfadden | Session: O02 – Evidence-Based Approaches for Optimizing Pharmacologic Treatment for Narcolepsy Session Date/Time: Monday, October 23, 9:00-10:30 AM |

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| Cardiovascular Burden of Patients Diagnosed With Idiopathic Hypersomnia: Real-World Idiopathic Hypersomnia Total Health Model (CV-RHYTHM) | R Saad | Session: O30 – Excessive Daytime Sleepiness: Detection, Assessment and Consequences Session Date/Time: Wednesday, October 25, 3:00-4:00 PM |
| Poster Presentations | | |
| Higher Healthcare Resource Utilization and Costs Among Patients With Idiopathic Hypersomnia Versus Matched Controls | R Saad | Poster board number: 062 Session: P1 Session Date/Time: Sunday, October 22, 5:00-6:00 PM |
| Effects of Oxybate on Sleep, Sleep Architecture, and Disrupted Nighttime Sleep | T Roth | Poster board number: 111 Session: P1 Session Date/Time: Sunday, October 22, 5:00-6:00 PM |
| Sodium Intake and Health Outcomes: A Systematic Review of Systematic Reviews | C Drachenberg | Poster board number: 303 Session: P1 Session Date/Time: Sunday, October 22, 5:00-6:00 PM |
| Clinical Comorbidities of Patients With Idiopathic Hypersomnia and Narcolepsy: A US Claims-Based Analysis | R Saad | Poster board number: 065 Session: P2 Session Date/Time: Monday, October 23, 6:00-7:00 PM |
| A Narcolepsy Detection Paradigm: Automated Nocturnal Detection and Notification of Sleep Onset Rapid Eye Movement Periods | A Cairns | Poster board number: 104 Session: P2 Session Date/Time: Monday, October 23, 6:00-7:00 PM |
| Insights From Real-World and Interventional Studies of Patients Transitioning From Sodium Oxybate to Low-Sodium Oxybate | W Macfadden | Poster board number: 111 Session: P2 Session Date/Time: Monday, October 23, 6:00-7:00 PM |
| Burden of Pediatric Narcolepsy on Patients and Caregivers | D Nichols | Poster board number: 114 Session: P2 Session Date/Time: Monday, October 23, 6:00-7:00 PM |
| Minimal Clinically Important Difference for the Visual Analog Scale for Sleep Inertia Using Data From a Phase 3 Trial of Low-Sodium Oxybate for Idiopathic Hypersomnia | R Bogan | Poster board number: 606 Session: P2 Session Date/Time: Monday, October 23, 6:00-7:00 PM |
| Economic Burden of Two Neurological Sleep Disorders: A US Claims Based Analysis of Idiopathic Hypersomnia and Narcolepsy | R Saad | Poster board number: 069 Session: P3 Session Date/Time: Tuesday, October 24, 6:00-7:00 PM |
| Blood Pressure Changes After Treatment With Low-Sodium Oxybate in Oxybate-Naive Patients With Narcolepsy or Idiopathic Hypersomnia: A Post Hoc Analysis | W Macfadden | Poster board number: 100 Session: P3 Session Date/Time: Tuesday, October 24, 6:00-7:00 PM |

Additionally, data from the following investigator-sponsored trials will be presented as poster presentations:

| Presentation Title | Lead Author | Session Number & Title / Date & Time (BRT) / Presentation Number |
|---|-------------|--|
| Toeing the Line: Exploring Diagnostic Uncertainty Along the Type 2 Narcolepsy-Idiopathic Hypersomnia Spectrum | C Clark | Poster board number: 104 Session: P1 Session Date/Time: Sunday, October 22, 5:00-6:00 PM |

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|--|---------|--|
| Diagnosis or Identity? Exploring Psychological Comorbidity Among Borderline Narcolepsy-Idiopathic Hypersomnia Patients | C Clark | Poster board number: 105 Session: P2 Session Date/Time: Monday, October 23, 6:00-7:00 PM |
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About Narcolepsy

Narcolepsy is a chronic, debilitating neurologic sleep disorder characterized by excessive daytime sleepiness (the inability to stay awake and alert during the day resulting in the irrepressible need to sleep or unplanned lapses into sleep or drowsiness), or EDS, and an inability to regulate sleep-wake cycles normally.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, therefore EDS is lifelong and has 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, nightly treatment, early access to an effective, low-sodium treatment can transform lives and reduce a patient's cardiovascular risk.⁵

About Idiopathic Hypersomnia

Idiopathic hypersomnia is a distinct, neurologic sleep disorder that goes beyond chronic excessive daytime sleepiness.^{10,11,12,13} Idiopathic hypersomnia occurs in an unrelenting 24-hour cycle, and symptoms may include a prolonged but non-restorative nighttime sleep episode of more than 9 hours, or a 24-hour sleep duration of 11 hours or longer, profound sleep inertia (prolonged difficulty waking, with frequent reentries into sleep, confusion, and irritability), cognitive impairment, long and unrefreshing naps and excessive daytime sleepiness that persists throughout the day.^{10,11,12,13,14} Although there are overlapping clinical features with narcolepsy, idiopathic hypersomnia is a condition with its own specific diagnostic criteria.^{13,15}

Idiopathic hypersomnia is a debilitating illness that can severely limit patients' occupational, familial and social 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 a low-sodium oxybate approved by the U.S. Food and Drug Administration (FDA) for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy. The FDA recognized seven years of Orphan Drug Exclusivity for Xywav in June 2021 for the treatment of cataplexy or excessive daytime sleepiness 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 excessive daytime sleepiness 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. 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. Xywav is the only low-sodium oxybate therapy approved by the FDA, and the only oxybate that does not carry a warning in the label related 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 in December 2021 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 excessive daytime sleepiness, 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: Taking XYWAV with other central nervous system (CNS) depressants such as medicines used to make you or your child fall asleep, including opioid analgesics, benzodiazepines, sedating antidepressants, antipsychotics, sedating anti-epileptic medicines, general anesthetics, muscle relaxants, alcohol, or street drugs, may cause serious medical problems, including trouble breathing (respiratory depression), low blood pressure (hypotension), changes in alertness (drowsiness), fainting (syncope), and death.

The active ingredient of XYWAV is a form of gamma-hydroxybutyrate (GHB). Abuse or misuse of illegal GHB alone or with other drugs that cause changes in alertness (or consciousness) has caused serious side effects. These effects include seizures, trouble breathing (respiratory depression), changes in alertness (drowsiness), coma, and death. Call your doctor right away if you or your child has any of these serious side effects.

Because of these risks, you have to go through the XYWAV and XYREM REMS to have your or your child's prescription for XYWAV filled.

Do not take XYWAV if you take or your child takes other sleep medicines or sedatives (medicines that cause sleepiness), drinks alcohol, or has a rare problem called succinic semialdehyde dehydrogenase deficiency.

Keep XYWAV in a safe place to prevent abuse and misuse. Selling or giving away XYWAV may harm others, and is against the law. Tell your doctor if

you have ever abused or been dependent on alcohol, prescription medicines, or street drugs.

Anyone who takes XYWAV should not do anything that requires them to be fully awake or is dangerous, including driving a car, using heavy machinery, or flying an airplane, for at least 6 hours after taking XYWAV. Those activities should not be done until you know how XYWAV affects you or your child.

XYWAV can cause serious side effects, including the following:

- **Breathing problems, including** slower breathing, trouble breathing, and/or short periods of not breathing while sleeping (sleep apnea). People who already have breathing or lung problems have a higher chance of having breathing problems when they use XYWAV.
- **Mental health problems, including** confusion, seeing or hearing things that are not real (hallucinations), unusual or disturbing thoughts (abnormal thinking), feeling anxious or upset, depression, thoughts of killing yourself or trying to kill yourself, increased tiredness, feelings of guilt or worthlessness, or difficulty concentrating. Tell your doctor if you or your child have or had depression or have tried to harm yourself or themselves. **Call your doctor right away if you have or your child has symptoms of mental health problems or a change in weight or appetite.**
- **Sleepwalking.** XYWAV can cause sleepwalking, which can cause injuries. Call your doctor if this occurs.

The most common side effects of XYWAV in adults include nausea, headache, dizziness, anxiety, insomnia, decreased appetite, excessive sweating (hyperhidrosis), vomiting, diarrhea, dry mouth, parasomnia (a sleep disorder that can include abnormal dreams, abnormal rapid eye movement (REM) sleep, sleep paralysis, sleep talking, sleep terror, sleep-related eating disorder, sleep walking, and other abnormal sleep-related events), somnolence, fatigue, and tremor.

The most common side effects of XYREM (which also contains oxybate like XYWAV) in children include nausea, bedwetting, vomiting, headache, weight decrease, decreased appetite, dizziness, and sleepwalking.

XYWAV can cause physical dependence and craving for the medicine when it is not taken as directed. These are not all the possible side effects of XYWAV.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full Prescribing Information, including Boxed Warning, here: <https://pp.jazzpharma.com/pi/xywav.en.USPI.pdf>

About Xyrem® (sodium oxybate) oral solution

Xyrem oral solution, CIII, is a product approved by the U.S. Food and Drug Administration (FDA) for both cataplexy and excessive daytime sleepiness in narcolepsy in adult and pediatric patients ages 7 and older.²⁴ Xyrem may only be dispensed to patients enrolled in the XYWAV and XYREM REMS. Xyrem was first approved in the U.S. in 2002, based on clinical trial data in adults.

Important Safety Information for Xyrem

WARNING: Taking XYREM with other CNS depressants such as medicines used to make you or your child fall asleep, including opioid analgesics, benzodiazepines, sedating antidepressants, antipsychotics, sedating anti-epileptic medicines, general anesthetics, muscle relaxants, alcohol, or street drugs, may cause serious medical problems, including trouble breathing (respiratory depression), low blood pressure (hypotension), changes in alertness (drowsiness), dizziness (syncope), and death.

XYREM is a form of gamma hydroxybutyrate (GHB). Abuse or misuse of illegal GHB alone or with other drugs that cause changes in alertness (or consciousness) has caused serious side effects. These effects include seizures, trouble breathing (respiratory depression), changes in alertness (drowsiness), coma, and death.

Because of these risks, you have to go through the XYWAV and XYREM REMS to have your or your child's prescription for XYREM filled.

Do not take XYREM if you take or your child takes other sleep medicines or sedatives (medicines that cause sleepiness), drink alcohol, or have a rare problem called succinic semialdehyde dehydrogenase deficiency.

Keep XYREM in a safe place to prevent abuse and misuse. Selling or giving away XYREM may harm others and is against the law. Tell your doctor if you have ever abused or been dependent on alcohol, prescription medicines, or street drugs.

Anyone who takes XYREM should not do anything that requires them to be fully awake or is dangerous, including driving a car, using heavy machinery, or flying an airplane, for at least 6 hours after taking XYREM. Those activities should not be done until you know how XYREM affects you or your child.

XYREM can cause serious side effects, including the following:

- **Breathing problems, including** slower breathing, trouble breathing, and/or short periods of not breathing while sleeping (sleep apnea). People who already have breathing or lung problems have a higher chance of having breathing problems when they use XYREM.
- **Mental health problems,** including confusion, seeing or hearing things that are not real (hallucinations), unusual or disturbing thoughts (abnormal thinking), feeling anxious or upset, depression, or thoughts of killing yourself or trying to kill yourself. Tell your doctor if you or your child have or had depression or have tried to harm yourself. **Call your doctor right away if you have or your child has symptoms of mental health problems.**
- **Sleepwalking.** Sleepwalking can cause injuries. Call your doctor if you or your child starts sleepwalking. Your doctor should check you or your child.

Tell your doctor if you are or your child is on a salt-restricted diet or if you have or your child has high blood pressure, heart failure, or kidney problems. XYREM contains a lot of sodium (salt) and may not be right for you or your child.

The most common side effects of XYREM include nausea, somnolence, dizziness, vomiting, bedwetting, and tremor (in adults). In pediatric patients, headache, decreased appetite, and weight decrease were also common. Your side effects may increase when you take higher doses of XYREM. XYREM can cause physical dependence and craving for the medicine when it is not taken as directed. These are not all the possible side effects of XYREM.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please find full prescribing information here: <http://pp.jazzpharma.com/pi/xyrem.en.USPI.pdf>

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc (NASDAQ: JAZZ) is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases—often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we are identifying new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. Please visit www.jazzpharmaceuticals.com for more information.

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