



Jazz Pharmaceuticals Announces Orphan Drug Exclusivity for Xywav™ (calcium, magnesium, potassium, and sodium oxybates) Oral Solution

June 25, 2021

U.S. Food and Drug Administration 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 safety compared to Xyrem® (sodium oxybate)

Xywav contains 92% less sodium per nightly dose than sodium oxybate

DUBLIN, June 25, 2021 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the U.S. Food and Drug Administration (FDA) has recognized seven years of Orphan Drug Exclusivity for Xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. Xywav is an oxybate product with a unique composition of cations resulting in 92% less sodium – or approximately 1,000 to 1,500 mg/night – than sodium oxybate at the recommended dosage range of 6 to 9 grams.¹

FDA also [published](#) its summary of clinical superiority findings for Xywav for the treatment of cataplexy or EDS associated with narcolepsy, stating that "the active moiety, oxybate, was previously approved as Xyrem® (sodium oxybate) for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy." According to FDA, "Xywav (calcium, magnesium, potassium, and sodium oxybates) is clinically superior to Xyrem by means of greater safety because Xywav provides a greatly reduced chronic sodium burden compared to Xyrem." The FDA's summary also stated that "the differences in the sodium content of the two products at the recommended doses will be clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated."

"We are pleased that FDA has recognized the greater safety of Xywav by virtue of the greatly reduced chronic sodium burden. This action is consistent with FDA's long-established position on the benefits of reducing daily sodium intake," said Robert Iannone, M.D., M.S.C.E., executive vice president, research and development and chief medical officer of Jazz Pharmaceuticals. "As a long-time leader in sleep medicine, we are well aware of the many challenges facing patients living with narcolepsy, including the greater risk of cardiometabolic comorbidities, including obesity, hypertension, diabetes and hypercholesterolemia.^{2,3,4,5} We are encouraged that FDA recognized the benefits of reducing sodium in a chronic medication for these patients. We advanced low-sodium Xywav from concept to commercial availability, demonstrating Jazz's maturing capabilities and delivering a much-needed medicine for patients in critical need."

The FDA's Orphan Drug Designation program is designed to advance the development of drugs that treat a condition affecting 200,000 or fewer U.S. patients annually. The seven-year market exclusivity for Xywav began on July 21, 2020, the date of FDA approval.

More information about Xywav, including Full Prescribing Information and Medication Guide, is available here. <<http://pp.jazzpharma.com/pi/xywav.en.USPI.pdf>>

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

Xywav, also known as JZP258, is a lower-sodium oxybate approved by FDA for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy. It is an investigational product being evaluated for the treatment of adult patients with idiopathic hypersomnia. Xywav is comprised of a unique composition of cations resulting in 92% less sodium, or approximately 1,000 to 1,500 mg/night, than sodium oxybate at the recommended adult dosage range of 6 to 9 grams. While the exact mechanism of action of Xywav is unknown, it is hypothesized that the therapeutic effects of Xywav on cataplexy and excessive daytime sleepiness are mediated through GABA_B actions during sleep at noradrenergic and dopaminergic neurons, as well as at thalamocortical neurons. Xywav received Fast Track designation by FDA in September 2020 for the treatment of idiopathic hypersomnia. The FDA recently accepted for filing and granted Priority Review the supplemental New Drug Application (sNDA) for this indication and the PDUFA date is set for August 12, 2021.

Important Safety Information

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 Program 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.** Sleepwalking can cause injuries. Call your doctor if you or your child starts sleepwalking. Your doctor should check you or your child.

The most common side effects of Xywav in adults include headache, nausea, dizziness, decreased appetite, 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 [somnambulism], and abnormal sleep-related events), diarrhea, excessive sweating (hyperhidrosis), anxiety and vomiting.

The most common side effects of Xywav in children include bedwetting (enuresis), nausea, headache, vomiting, weight decrease, decreased appetite, dizziness and sleep walking.

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.

About Narcolepsy

Narcolepsy is a chronic, debilitating neurological disorder characterized by EDS and the inability to regulate sleep-wake cycles normally.^{6,7,8} It affects an estimated one in 2,000 people in the United States, with symptoms typically appearing in childhood or adolescence.^{9,10,11} Studies have shown it may take 10 years or more for people with narcolepsy to receive a diagnosis.^{12,13} There are five main symptoms of narcolepsy, including EDS, cataplexy, disrupted nighttime sleep, sleep-related hallucinations, and sleep paralysis.¹⁴ While all people with narcolepsy experience EDS, not all individuals with narcolepsy experience all five symptoms.^{7,13} EDS is the primary symptom of narcolepsy and is present in all people with the disorder.^{11,15} EDS is characterized by the inability to stay awake and alert during the day resulting in drowsiness and unplanned lapses into sleep.^{9,11,12} Narcolepsy is associated with an increased prevalence of cardiometabolic comorbidities, including obesity, hypertension, diabetes and hypercholesterolemia.^{2,3,4,5}

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. We actively explore new options for patients including novel compounds, small molecules and biologics, and through cannabinoid science and innovative delivery technologies. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. For more information, please visit www.jazzpharmaceuticals.com and follow @JazzPharma on Twitter.

Caution Concerning Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, belief in the potential of Xywav to make a difference for people living with narcolepsy and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2020 and future filings and reports by Jazz Pharmaceuticals. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect Jazz Pharmaceuticals' forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

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