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

Letter of Medical Necessity Template: Indication for Cataplexy or EDS in Narcolepsy

Jazz Pharmaceuticals

[To be placed on physician/provider letterhead]

TO: **[Medical Director]**
[Insurance Company]
[Address]
[City, State, ZIP]

RE: **[Patient Name]**
[Policy ID Number]
[Policy Group]
[Patient Date of Birth]

Dear Dr. **[Last Name]**:

I am writing this letter on behalf of my patient, **[insert patient name]**, to request coverage for XYWAV® (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII, 0.5 g/mL total salts (equivalent to 0.413 g/mL of oxybate) to treat **[insert diagnosis]**. XYWAV (NDC #68727-150-01) is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.[1]

[Optional] The FDA has determined XYWAV to be clinically superior to XYREM® (sodium oxybate) oral solution, indicating in their summary[2,a]:

- "XYWAV is clinically superior to XYREM by means of greater safety because XYWAV provides a greatly reduced chronic sodium burden"
- "The differences in the sodium content between XYWAV and XYREM at the recommended doses will be clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated"

[a]The decision of the FDA OOPD is based on findings that XYWAV provides a greatly reduced chronic sodium burden compared to XYREM.[2] There are no head-to-head data for XYWAV and XYREM.

[Optional] I also request that my appeal be reviewed by

- A physician adviser not involved in the original decision
- A board-certified sleep medicine physician

Treatment of **[insert patient name]** with XYWAV is medically appropriate and necessary. This letter outlines the patient's medical history, prognosis, and treatment rationale.

1) Medical History and Prognosis

- **[Patient's diagnosis, condition, and medical history, including any history of cardiovascular comorbidities, diabetes, anxiety, or sodium intake restraints]**
- **[Previous therapies for the symptoms associated with the patient's condition and the patient's response to these therapies, as well as current therapies for patients being actively treated]**
- **[Brief description of the patient's recent symptoms and conditions]**

2) Rationale for Treatment

- **[Summary of why, based on your clinical judgment, your patient requires treatment with XYWAV]**

[Optional] For most adults in the general population, the American Heart Association currently recommends aiming for a reduced intake of dietary sodium of at least 1000 mg/day if the optimal goal of a dietary sodium intake of less than 1500 mg/day cannot be attained.[3,4] Compared with sodium oxybate, XYWAV is a lower-sodium oxybate.[5]

Please call my office at **[insert telephone number]** if I can provide you with any additional information. I look forward to receiving your timely response and approval.

Sincerely,

[Insert healthcare provider name and participating provider phone number]

Enclosures (as appropriate): Prior authorization form, office notes, documentation of prior medication history, test results, clinical peer-reviewed literature, XYWAV package insert.

FDA=US Food and Drug Administration; MSLT=multiple sleep latency test; NDC=National Drug Code; OOPD=Office of Orphan Products Development.

References: 1. XYWAV [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **2.** Clinical superiority findings. US Department of Health and Human Services. US Food and Drug Administration website. https://www.fda.gov/industry/designatingorphan-product-drugs-and-biological-products/clinical-superiority-findings. Updated June 24, 2021. Accessed October 14, 2021. **3.** Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:e13-e115. **4.** Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140:e563-e595. **5.** Bogan RK, Thorpy MJ, Dauvilliers Y, et al. Efficacy and safety of calcium, magnesium, potassium, and sodium oxybates (lower-sodium oxybate [LXB]; JZP-258) in a placebo-controlled, double-blind, randomized withdrawal study in adults with narcolepsy with cataplexy. *Sleep*. 2021;44(3):zsaa206.

Please see next page for Important Safety Information and accompanying full Prescribing Information, including BOXED Warning, or click here for full PI.

Indications and Usage

XYWAV® (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII, 0.5 g/mL total salts (equivalent to 0.413 g/mL of oxybate), is indicated for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy.

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 narcolepsy 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

- CNS Depression: Use caution when considering the concurrent use with other CNS depressants. If concurrent use is required, consider dose reduction or discontinuation of one or more CNS depressants (including XYWAV). Consider interrupting XYWAV treatment if short-term opioid use is required. After first initiating treatment and until certain that XYWAV does not affect them adversely, 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 III controlled substance. 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).
- 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 pivotal clinical trial in adult patients with narcolepsy (n=201), depression and depressed mood were reported in patients treated with XYWAV. In most cases, no change in XYWAV treatment was required. 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. Monitor patients for the emergence of increased depressive symptoms and/or suicidality while taking XYWAV, which require careful and immediate evaluation.
- Other Behavioral or Psychiatric Adverse Reactions: Monitor patients for impaired motor/cognitive function or the emergence of or increase in anxiety and/or confusion. The emergence or increase in the occurrence of behavioral or psychiatric events in patients taking XYWAV should be carefully monitored.
- Parasomnias: In pivotal clinical trials, parasomnias including sleepwalking were reported in adult patients treated with XYWAV. Parasomnias, including sleepwalking, also 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

In Study 1, the most common adverse reactions (incidence ≥5% of XYWAV-treated patients) were headache, nausea, dizziness, decreased appetite, parasomnia, diarrhea, hyperhidrosis, anxiety, and vomiting.

In the pediatric clinical trial with XYREM (same active moiety as XYWAV) in patients 7 years of age and older 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 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.

Please see accompanying full Prescribing Information, including BOXED Warning, or click here for full PI.