

THE
FIRST
& ONLY

Lumryz™

(sodium oxybate) for extended-release
oral suspension 

The first and only single-dose sodium oxybate¹

Your quick guide to starting patients on
once-at-bedtime LUMRYZ after enrollment in
the LUMRYZ REMS and RYZUP™ Support Services¹⁻³

Patients experiencing inadequate treatment response on their current medication may benefit from help with daytime symptom control of excessive daytime sleepiness (EDS) and cataplexy with a single-dose sodium oxybate.



Currently taking
twice-nightly
oxybate



Oxybate-naïve
or previous
oxybate history

REMS, Risk Evaluation and Mitigation Strategy.

IMPORTANT SAFETY INFORMATION

WARNING: CENTRAL NERVOUS SYSTEM (CNS) DEPRESSION AND ABUSE AND MISUSE

Central Nervous System Depression

LUMRYZ™ (sodium oxybate) is a CNS depressant. Clinically significant respiratory depression and obtundation may occur in patients treated with LUMRYZ at recommended doses. Many patients who received LUMRYZ during clinical trials in narcolepsy were receiving CNS stimulants.

Abuse and Misuse

LUMRYZ (sodium oxybate) is the sodium salt of 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, decreased consciousness, coma, and death.

Because of the risks of CNS depression and abuse and misuse, LUMRYZ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the LUMRYZ REMS.

INDICATIONS AND USAGE

LUMRYZ (sodium oxybate) for extended-release oral suspension is a central nervous system depressant indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.

CONTRAINDICATIONS

LUMRYZ is contraindicated for use in:

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

WARNINGS AND PRECAUTIONS

Central Nervous System Depression

The concurrent use of LUMRYZ with other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating antiepileptic 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 LUMRYZ is required, dose reduction or discontinuation of one or more CNS depressants (including LUMRYZ) should be considered. In addition, if short-term use of an opioid (eg, post- or perioperative) is required, interruption of treatment with LUMRYZ should be considered.

After first initiating treatment and until certain that LUMRYZ does not affect them adversely (eg, impair judgment, thinking, or motor skills), caution patients against engaging in hazardous activities requiring complete mental alertness or motor coordination such as operating hazardous machinery, including automobiles or airplanes. Also caution patients against engaging in these hazardous activities for at least six (6) hours after taking LUMRYZ. Patients should be queried about CNS depression-related events upon initiation of LUMRYZ therapy and periodically thereafter.

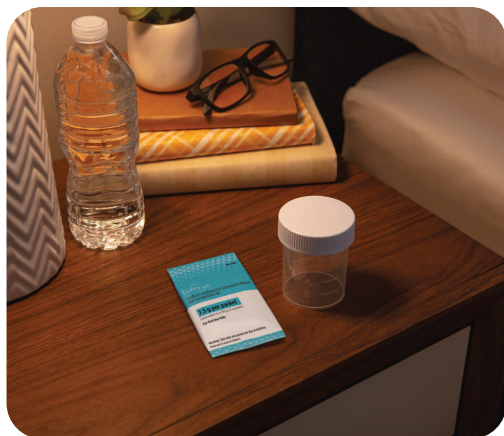
Abuse and Misuse

LUMRYZ is a Schedule III controlled substance. The active ingredient of LUMRYZ, sodium oxybate, is the sodium salt of 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 amnesic 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 Important Safety Information, including BOXED Warning, throughout and the accompanying full Prescribing Information, and Medication Guide, or visit LUMRYZhcp.com.

Patients can reliably receive a consistent full dose with LUMRYZ¹

Premeasured packets streamline dosing to ensure patients consistently receive full therapeutic effects of their prescribed dose^{1,4}



Instruct patients to take once-at-bedtime LUMRYZ by^{1,5}:

- Combining their premeasured dose and 1/3 cup of water in the provided mixing cup
 - Patients should **not** use hot water
- Shaking for at least **60 seconds (1 minute)** before drinking, drink within **30 minutes** of mixing
- Immediately refilling the mixing cup to Line B, then shake for **10 seconds** and take again to ensure all medication was consumed

LUMRYZ should be taken in bed at least 2 hours after eating, as patients often fall asleep within 5-15 minutes of taking their dose without feeling drowsy.¹

- Please advise your patient to read the FDA-approved Medication Guide and Instructions for Use for complete instructions



Available dose strengths are 4.5 g, 6 g, 7.5 g, and 9 g¹



LUMRYZ can be taken concomitantly with stimulants¹



Premeasured dose packets allow for convenient travel¹

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

LUMRYZ REMS

LUMRYZ is available only through a restricted distribution program called the LUMRYZ REMS because of the risks of central nervous system depression and abuse and misuse.

Notable requirements of the LUMRYZ REMS include the following:

- Healthcare providers who prescribe LUMRYZ are specially certified.
- LUMRYZ will be dispensed only by pharmacies that are specially certified.
- LUMRYZ will be dispensed and shipped only to patients who are enrolled in the LUMRYZ REMS with documentation of safe use conditions.

Further information is available at www.LUMRYZREMS.com or by calling 1-877-453-1029.

Respiratory Depression and Sleep-Disordered Breathing

LUMRYZ may impair respiratory drive, especially in patients with compromised respiratory function. In overdoses of oxybate with illicit use of GHB, life-threatening respiratory depression has been reported. Increased apnea and reduced oxygenation may occur with LUMRYZ administration. A significant increase in the number of central apneas and clinically significant oxygen desaturation may occur in patients with obstructive sleep apnea treated with LUMRYZ. 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

Depression, and suicidal ideation and behavior, can occur in patients treated with LUMRYZ. In an adult clinical trial in patients with narcolepsy (n=212), there were no suicide attempts, but one patient with a history of depression and anxiety developed suicidal ideation in the LUMRYZ-treated patients. The emergence of depression in patients treated with LUMRYZ requires careful and immediate evaluation. Patients with a previous history of a depressive illness and/or a suicide attempt should be monitored carefully for the emergence of depressive symptoms while taking LUMRYZ.

Other Behavioral or Psychiatric Adverse Reactions

Other behavioral and psychiatric adverse reactions can occur in patients taking LUMRYZ. During adult clinical trials in patients with narcolepsy administered LUMRYZ, 2% of 107 patients treated with LUMRYZ experienced a confusional state. No patients treated with LUMRYZ discontinued treatment because of confusion. Anxiety occurred in 7.5% of 107 patients treated with LUMRYZ in the adult trial in patients with narcolepsy. Other psychiatric reactions reported in adult clinical trials in patients with narcolepsy administered LUMRYZ included irritability, emotional disorder, panic attack, agitation, delirium, and obsessive thoughts. Other neuropsychiatric reactions reported in adult clinical trials in patients with narcolepsy administered immediate-release sodium oxybate and in the postmarketing setting for immediate-release sodium oxybate include hallucinations, paranoia, psychosis, aggression, and agitation. The emergence or increase in the occurrence of behavioral or psychiatric events in patients taking LUMRYZ should be carefully monitored.

Please see Important Safety Information, including BOXED Warning, throughout and the accompanying full Prescribing Information, and Medication Guide, or visit LUMRYZhcp.com.

How might once-at-bedtime LUMRYZ make an impact for patients in your practice?

Switching from twice-nightly sodium oxybate¹

To switch patients from an immediate-release sodium oxybate, **select the nearest equivalent dose of LUMRYZ in grams per night.**

- For example, **7.5 g of LUMRYZ** is approximately **2 doses of 3.75 g twice-nightly** sodium oxybate

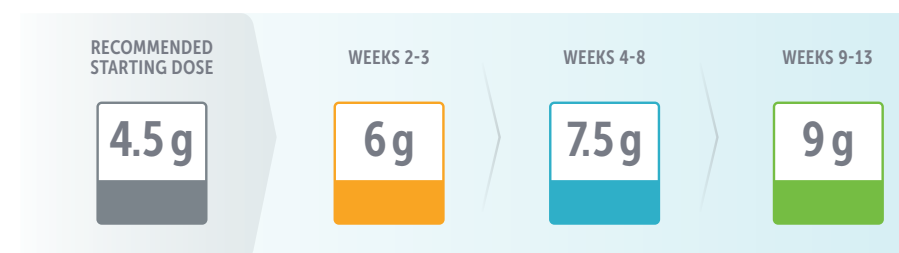


Results from a qualitative study of patient perspectives suggest that waking up to take a second dose is a source of stress for patients, who also report sometimes missing the second dose of treatment as prescribed.^{6-8*}

Starting LUMRYZ for new patients or those with previous history on oxybates¹

LUMRYZ should be titrated to a dose that best fits your patients' needs. Increase the recommended starting dose of 4.5 g by **1.5 g per night at weekly intervals as needed**, based on efficacy and tolerability.

PIVOTAL CLINICAL TRIAL DOSING SCHEDULE²:



Doses higher than 9 g per night have not been studied and should not ordinarily be administered.

*Based on a qualitative study of 75 patients with experience taking twice-nightly sodium oxybate. Participants were asked to rate statements about the burden of narcolepsy on a scale of 1-9, where 1="completely disagree" and 9="completely agree."

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

Parasomnias

Parasomnias can occur in patients taking LUMRYZ. Sleepwalking, defined as confused behavior occurring at night and at times associated with wandering, was reported in 3% of 107 patients with narcolepsy treated with LUMRYZ. No patients treated with LUMRYZ discontinued due to sleepwalking. Episodes of sleepwalking should be fully evaluated and appropriate interventions considered.

Use in Patients Sensitive to High Sodium Intake

LUMRYZ has a high sodium content. In patients sensitive to sodium intake (eg, those with heart failure, hypertension, or renal impairment), consider the amount of daily sodium intake in each dose of LUMRYZ.

MOST COMMON ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5% and greater than placebo) reported for any dose of LUMRYZ were nausea, dizziness, enuresis, headache, and vomiting.

ADDITIONAL ADVERSE REACTIONS

Additional adverse reactions that occurred in ≥2% of patients treated with LUMRYZ and were more frequent in the LUMRYZ treatment group than with placebo were vomiting, nausea, decreased weight, decreased appetite, dizziness, somnolence, headache, enuresis, anxiety, and somnambulism.

DRUG INTERACTIONS

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

Please see Important Safety Information, including BOXED Warning, throughout and the accompanying full Prescribing Information, and Medication Guide, or visit LUMRYZhcp.com.

PREGNANCY AND LACTATION

There are no adequate data on the developmental risk associated with the use of sodium oxybate in pregnant women. LUMRYZ 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 LUMRYZ and any potential adverse effects on the breastfed infant from LUMRYZ or from the underlying maternal condition.

PEDIATRIC USE

Safety and effectiveness of LUMRYZ in pediatric patients have not been established.



(sodium oxybate) for extended-release oral suspension

LUMRYZ is once at bedtime, for their daytime¹

FDA has determined LUMRYZ™ to be clinically superior to twice-nightly oxybates^{9*}

Once-at-bedtime LUMRYZ dosing was found to be a major contribution to patient care over both Xyrem® (sodium oxybate) and Xywav® (calcium, magnesium, potassium and sodium oxybates) indicating that:

- LUMRYZ once-at-bedtime dosing does not involve disrupting or fragmenting sleep, whereas Xyrem and Xywav necessitate a nocturnal awakening to take a second dose that disrupts sleep architecture
- LUMRYZ is “inherently more convenient, easier, and less burdensome for patients to forgo awakening to take a second dose on a nightly basis, especially given that narcolepsy is a chronic neurologic condition.”

Help provide daytime symptom control of excessive daytime sleepiness and cataplexy with a single-dose sodium oxybate^{1,2,4}

Start or switch your patients on the appropriate single dose of LUMRYZ.¹



Need to enroll your patient in RYZUP™?

Scan or visit [RYZUPSupport.com/iassist](https://www.ryzup.com/iassist) to start the process.

*Based on a determination of Orphan Drug Exclusivity by the FDA Office of Orphan Products Development (OOPD) between LUMRYZ and Xyrem or Xywav. There are no head-to-head data for LUMRYZ and Xyrem or Xywav.

IMPORTANT SAFETY INFORMATION

GERIATRIC USE

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

LUMRYZ should not be initiated in patients with hepatic impairment because appropriate dosage adjustments for initiation cannot be made with the available dosage strengths. Patients with hepatic impairment who have been titrated to a maintenance dosage of another oxybate product can be switched to LUMRYZ if the appropriate dosage strength is available.

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 three (3) to fourteen (14) days. In cases of severe withdrawal, hospitalization may be required. The discontinuation effects of LUMRYZ have not been systematically evaluated in controlled clinical trials. Tolerance to LUMRYZ 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 LUMRYZ dosage regimen.

Please see Important Safety Information, including BOXED Warning, throughout and the accompanying full Prescribing Information, and Medication Guide, or visit [LUMRYZhcp.com](https://www.lumryzhcp.com).

References: **1.** LUMRYZ. Package insert. Chesterfield, MO: Avadel Pharmaceuticals; 2023. **2.** Kushida CA, Shapiro CM, Roth T, et al. Once-nightly sodium oxybate (FT218) demonstrated improvement of symptoms in a phase 3 randomized clinical trial in patients with narcolepsy. *Sleep*. 2022;45(6):1-11. doi:10.1093/sleep/zsab200 **3.** Abad VC. An evaluation of sodium oxybate as a treatment option for narcolepsy. *Expert Opin Pharmacother*. 2019;20(10):1189-1199. doi:10.1080/14656566.2019.1617273 **4.** Bogan R, Thorpy MJ, Winkelman JW, et al. Randomized, crossover, open-label study of the relative bioavailability and safety of FT218, a once-nightly sodium oxybate formulation: Phase 1 study in healthy volunteers. *Sleep Med*. 2022; 100:442-447. **5.** LUMRYZ Instructions for Use. Chesterfield, MO: Avadel Pharmaceuticals; 2023. **6.** XYREM. Package insert. Palo Alto, CA: Jazz Pharmaceuticals, Inc; 2022. **7.** XYWAV. Package insert. Palo Alto, CA: Jazz Pharmaceuticals, Inc; 2022. **8.** Dubow J, Avidan AY, Corsier B, et al. Preferences for attributes of sodium oxybate treatment: a discrete choice experiment in patients with narcolepsy. *Patient Prefer Adherence*. 2022; 16:937-947. doi:10.2147/PPA.S353412 **9.** US Food and Drug Administration. Clinical Superiority Findings. Accessed May 01, 2023. <https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/clinical-superiority-findings#644fe8ebd4a58>