



ONCE AT
BEDTIME
Lumryz™

(sodium oxybate) for extended-release
oral suspension 4.5 | 6 | 7.5 | 9 g

IDENTIFYING PATIENTS TO **SWITCH AND START** ON LUMRYZ

Follow 3 people with narcolepsy on their journey
to starting with once-at-bedtime LUMRYZ.

Patients were compensated by Avadel Pharmaceuticals to share their stories.
Individual results may vary.

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 patients 7 years of age and older with narcolepsy.

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.

CONTRAINDICATIONS

LUMRYZ is contraindicated for use in:

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

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



Meet Wendy:

Living with NT1, switched to LUMRYZ

Wendy's treatment journey

Wendy's first cataplexy attack

"I was laughing and jumping on the bed, and then dropped to the floor. After I could move again, I told my mother. She thought I was making it up."

AGE 12

Wendy is told her symptoms are psychosomatic

"I spent a week in the hospital after a cataplexy attack and was told nothing was wrong with me. I thought everybody was right and I knew nothing."

EDS, excessive daytime sleepiness; NT1, narcolepsy type 1.

IMPORTANT SAFETY INFORMATION (cont'd)

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-

Wendy is diagnosed with narcolepsy

"After 25 years and so many misdiagnoses, I was told I had narcolepsy and was put on a stimulant to treat my EDS."

AGE 37

Wendy struggles to find the right treatment regimen

"Every 6 months we would raise the dose or switch to another stimulant. They helped me stay awake—but staying awake meant being in a fog all the time. And I was still having symptoms of cataplexy."

Wendy starts researching oxybate therapies.

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.

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WENDY TODAY



Since starting once-at-bedtime LUMRYZ, I feel less sleepy and more awake during the day. I can watch movies with my husband and paint without falling asleep and getting paint all over my clothes.



Wendy starts on twice-nightly sodium oxybate

"My doctor prescribed a twice-nightly oxybate. I woke up one day after taking it and for the first time in 8 years, I didn't have a cataplexy spell, I wasn't as sleepy. I was awake enough to attend my college classes. I finished my degree."

AGE 43

Wendy faces challenges due to EDS

"I kept struggling with the second dose and feeling sleepy the next day. Employers wouldn't recognize my hard work because I took so many naps. They thought I was lazy."

Wendy joins the LUMRYZ clinical trial

"After having trouble managing the middle-of-the-night dose for so long, I needed another option besides twice-nightly."

AGE 53



Do you have patients like Wendy who may benefit from switching to—or starting with—once-at-bedtime LUMRYZ?

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.



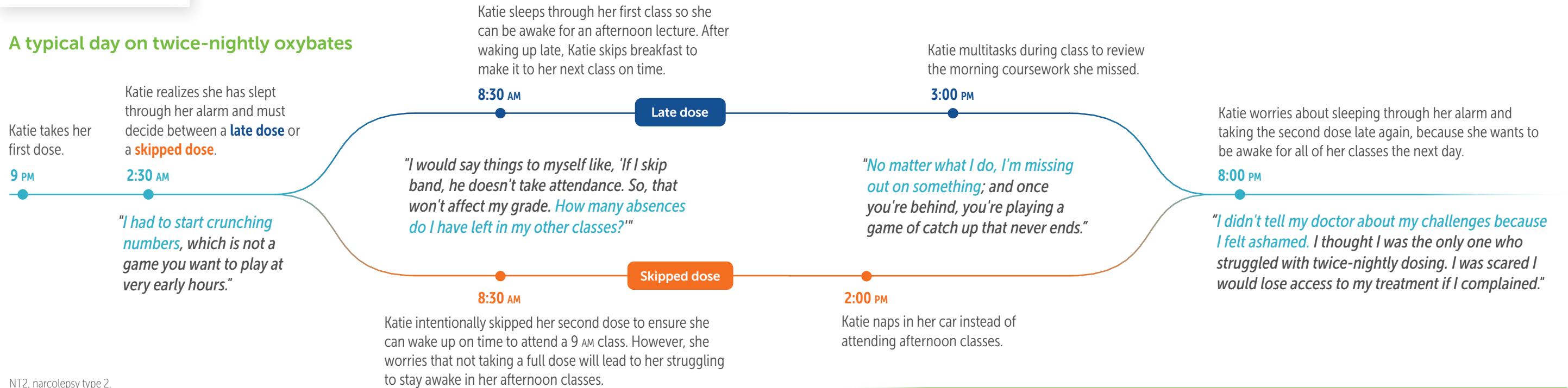
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Meet Katie:

Living with NT2, switched to LUMRYZ

A typical day on twice-nightly oxybates



NT2, narcolepsy type 2.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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

KATIE TODAY

"Once-at-bedtime LUMRYZ for me means I go to sleep and the only thing I have to think of is what I'm going to be doing the next day. I'm not falling asleep in the morning, so I like to make myself breakfast and drive to class."

? How are you maintaining an open dialogue with patients about the potential challenges with taking middle of the night dosing?

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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Meet Tyler:

Living with NT1, switched to LUMRYZ

Growing up with narcolepsy

"I was constantly sleepy, and 2 minutes into a basketball game my legs would start feeling like jelly. It was frustrating, because I had been planning to go to college on a sports scholarship."

"My mom mentioned I would nap while my friends played soccer outside, and that led my doctor to recommend a sleep study."

8TH GRADE

11TH GRADE

FIRST YEAR OF COLLEGE

"My sleep specialist recommended starting with twice-nightly sodium oxybate.

I noticed a difference soon after starting. I didn't struggle as much to stay awake while reading."

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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 group. In a clinical trial in pediatric narcolepsy patients administered

immediate-release sodium oxybate, one patient experienced suicidal ideation and two patients reported depression. 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.

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TYLER TODAY

"Since taking once-at-bedtime LUMRYZ, I feel awake when I spend time with friends and do my homework. My cataplexy attacks have also mitigated, so I'm not focused on my cataplexy when I play pick-up games of soccer or basketball.

Once-at-bedtime dosing for me means not relying on someone else to help me wake up in the middle of the night to take a second dose—now I have a roommate, and I'm not worried about waking them up every night.

"My mom had to wake me up every night, or else I wouldn't get up to take the second dose in the middle of the night as prescribed."

"When I started college, I had to have a single room so I wasn't burdening anyone else. But that also meant I had no one to help me take the middle-of-the-night dose."



Do you have patients like Tyler who may have family members who are impacted by their current treatment regimen?


IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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. In a clinical trial in pediatric patients administered immediate-release sodium oxybate, neuropsychiatric reactions including acute psychosis, confusion, and anxiety were reported. The emergence or increase in the occurrence of behavioral or psychiatric events in patients taking LUMRYZ should be carefully monitored.

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The LUMRYZ Starter Kit is available for titrating new patients

Start appropriate patients with 28 days of treatment in escalating dose strengths.¹



Each premeasured packet contains a full therapeutic dose.¹



No middle-of-the-night alarm clock^{1,5,6}



Convenient for packing and travel



No second dose left out unattended^{1,5,6}



Taken orally as a single dose at bedtime¹

- Can be taken concomitantly with alerting agents



Each dose contains a blend of immediate- and controlled-release granules^{1,2}

- Shake for 60 seconds—expect the granules to not fully dissolve in water* and have a gritty texture with a salty taste⁷



Should be taken at least 2 hours after eating and in bed¹

- Patients may fall asleep within 5-15 minutes of taking their dose without feeling drowsy

*Do not use hot water.

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use) for full administration instructions.

IMPORTANT SAFETY INFORMATION (cont'd)

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 adult 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.

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

Managing expectations for patients

Patients who are new to oxybate or who have discontinued oxybate treatment may have questions during their first few weeks of treatment with LUMRYZ.



Everyone responds to treatment differently

It may take time before your patients can see a difference in their EDS or cataplexy.

In the clinical trial for LUMRYZ, some participants saw significant symptom improvements as early as week 3, while others saw symptom improvements at week 13 after titrating to a higher dose.^{1,21}



Finding their stable dose takes time

It may take time to find the dose that best balances efficacy and tolerability for each patient.

In the clinical trial for LUMRYZ, side effects typically occurred when participants started a new dose. Generally, the side effects then declined over time while staying on the same dose.²



Consider frequent check-ins in the titration period

Encourage patients to share their experience with LUMRYZ to help determine if they might benefit from any adjustments to their dose.

¹As seen in participants taking the 9-g dose of LUMRYZ and compared to baseline results at the start of the trial.

The most common side effects reported by participants in the clinical trial include nausea, dizziness, bedwetting, headache, and vomiting. In pediatric patients, the most common side effects include nausea, bedwetting, vomiting, headache, weight decreased, decreased appetite, dizziness, and sleepwalking.¹

IMPORTANT SAFETY INFORMATION (cont'd)

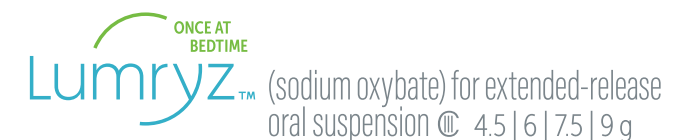
WARNINGS AND PRECAUTIONS (cont'd)

MOST COMMON ADVERSE REACTIONS

Most common adverse reactions (incidence >5% and greater than placebo) reported for any dose of LUMRYZ in a trial of adults with narcolepsy were nausea, dizziness, enuresis, headache, and vomiting. Similarly, in a trial of pediatric narcolepsy patients receiving immediate release sodium oxybate, the most commonly observed adverse reactions (incidence ≥5%) were nausea, enuresis, vomiting, headache, decreased weight, decreased appetite, dizziness, and sleepwalking.

ADDITIONAL ADVERSE REACTIONS

Additional adverse reactions that occurred in ≥2% of adult patients with narcolepsy 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.



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

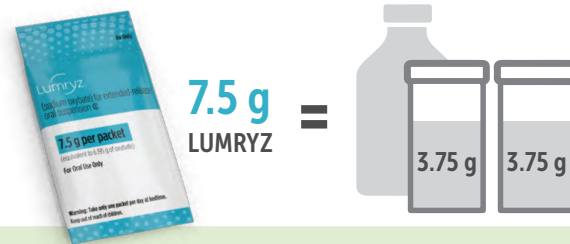
DOSING IN ADULTS

How might once-at-bedtime LUMRYZ make an impact for your patients' daytime?

SWITCH from twice-nightly oxybate

Select the nearest equivalent dose of LUMRYZ¹

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



IMPORTANT FOR SWITCH PATIENTS

It's important to know how often patients missed the second dose of their twice-nightly oxybate, as it may be more appropriate to switch to a lower starting dose of LUMRYZ than what they were previously prescribed. It may take time to find a stable dose. Remind patients it's important to share how they are feeling with your office during the titration process.

START patients new to oxybate or with previous oxybate history

Consider increasing the recommended starting dose of 4.5 g by 1.5 g per night at weekly intervals based on efficacy and tolerability.¹ Doses higher than 9 g per night have not been studied and should not ordinarily be administered.¹

IMPORTANT FOR STARTING LUMRYZ

Patients will start with the smallest dose, then adjust the strength up or down, slowly over time, based on efficacy and tolerability.^{1,8} It's important to let patients know that everybody responds to treatment differently and it may take time before they can see a difference in their EDS or cataplexy as their body adjusts to the medicine.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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.

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



DOSING IN PEDIATRIC PATIENTS

Once-at-bedtime LUMRYZ is the only single-dose oxybate approved for pediatric use (ages ≥ 7)¹

SWITCH pediatric patients ≥ 20 kg (44 lb)

Select the nearest equivalent dose of LUMRYZ¹

Switch patients to LUMRYZ if they are taking a 4.5-g dose or higher of another sodium oxybate. The dosage may be gradually titrated based on efficacy and tolerability.

START pediatric patients ≥ 45 kg (99 lb)

Titrate gradually to a dose that best fits their needs¹

Start on 4.5 g once per night and then increase by 1.5 g per night at weekly intervals to the maximum recommended dosage of 9 g per night orally.



What might it mean for family and care partners to **not wake to administer a middle-of-the-night dose?**

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

PEDIATRIC USE

LUMRYZ has not been studied in a pediatric clinical trial for narcolepsy. The safety and effectiveness of LUMRYZ in the treatment of cataplexy or excessive daytime sleepiness in pediatric patients 7 years of age and older with narcolepsy is supported by evidence from a double-blind, placebo-controlled, randomized-withdrawal study of immediate-release sodium oxybate. Safety and effectiveness of LUMRYZ in pediatric patients below the age of 7 years have not been established.

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.

ONCE AT BEDTIME
Lumryz™ (sodium oxybate) for extended-release oral suspension © 4.5 | 6 | 7.5 | 9 g

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Lumryz™ ONCE AT BEDTIME
 (sodium oxybate) for extended-release oral suspension  4.5 | 6 | 7.5 | 9 g



Once-at-bedtime LUMRYZ delivers therapeutic exposure over the course of a patient's nocturnal sleep period^{1,2,4}

- **Established safety and demonstrated efficacy** across 3 co-primary endpoints (MWT, CGI-I, weekly cataplexy attacks) and select secondary endpoint (ESS)²
- **Premeasured packets** contain a full therapeutic dose¹

MWT, Maintenance of Wakefulness Test; CGI-I, Clinical Global Impression - Improvement; ESS, Epworth Sleepiness Scale.

RYZUP™
 SUPPORT SERVICES

To get started, enroll your patient in RYZUP™ Support Services. Scan or visit RYZUPSupport.com/iasist



LUMRYZ is a single-dose oxybate for the treatment of EDS and cataplexy in patients 7 years of age and older with narcolepsy.¹

LUMRYZ is covered for **more than 90%** of commercially insured patients on all national plans.⁹

IMPORTANT SAFETY INFORMATION (cont'd)

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 throughout, and the accompanying full Prescribing Information, including BOXED WARNING, and Medication Guide, or visit LUMRYZhcp.com.

References: **1.** LUMRYZ™ (sodium oxybate for extended-release oral suspension). Prescribing Information. Chesterfield, MO: Avadel Pharmaceuticals. **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.** Thakrar C, Patel K, D'ancona G, et al. Effectiveness and side-effect profile of stimulant therapy as monotherapy and in combination in the central hypersomnias in clinical practice. *J Sleep Res*. 2018;27(4):e12627. doi:10.1111/jsr.12627 **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.** XYREM. Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc; 2023. **6.** XYWAV. Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc; 2023. **7.** LUMRYZ Instructions for Use. Chesterfield, MO: Avadel Pharmaceuticals; 2024. **8.** Caffrey AR, Borrelli EP. The art and science of drug titration. *Ther Adv Drug Saf*. 2020;11:2042098620958910. **9.** Avadel. Data on file.

