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

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.

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.

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 full Prescribing Information, including BOXED Warning, and Medication Guide available at LUMRYZhcp.com.

Meet Wendy:

Living with NT1, switched to LUMRYZ

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's treatment journey

AGE 12

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."

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."

AGE 37

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."

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.

AGE 43

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."

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."

AGE 53

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."

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

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

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.

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 amnestic 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.

ONCE AT BEDTIME
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Meet Katie:

Living with NT2, switched to LUMRYZ

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.***

A typical day on twice-nightly oxybates

9 PM — Katie takes her first dose.

2:30 AM — Katie realizes she has slept through her alarm and must decide between a **late dose** or a **skipped dose**.

"I had to start crunching numbers, which is not a game you want to play at very early hours."

Late dose

8:30 AM — Katie sleeps through her first class so she can be awake for an afternoon lecture. After waking up late, Katie skips breakfast to make it to her next class on time.

"I would say things to myself like, 'If I skip band, he doesn't take attendance. So, that won't affect my grade. How many absences do I have left in my other classes?'"

3:00 PM — Katie multitasks during class to review the morning coursework she missed.

"No matter what I do, I'm missing out on something; and once you're behind, you're playing a game of catch up that never ends."

8:00 PM — Katie worries about sleeping through her alarm and taking the second dose late again, because she wants to be awake for all of her classes the next day.

"I didn't tell my doctor about my challenges because I felt ashamed. I thought I was the only one who struggled with twice-nightly dosing. I was scared I would lose access to my treatment if I complained."

Skipped dose

8:30 AM — Katie intentionally skipped her second dose to ensure she can wake up on time to attend a 9 AM class. However, she worries that not taking a full dose will lead to her struggling to stay awake in her afternoon classes.

2:00 PM — Katie naps in her car instead of attending afternoon classes.

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.

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.

Please see Important Safety Information throughout, and full Prescribing Information, including BOXED Warning, and Medication Guide available at LUMRYZhcp.com.

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)

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.

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Meet Tyler:

Living with NT1, switched to LUMRYZ

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.__"

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."

"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."

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."

"It was a huge relief that my sleep specialist listened to me and heard my challenges with taking twice-nightly dosing so we could explore other options."

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. The emergence or increase in the occurrence of behavioral or psychiatric events in patients taking LUMRYZ should be carefully monitored.

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.

Please see Important Safety Information throughout, and full Prescribing Information, including BOXED Warning, and Medication Guide available at LUMRYZhcp.com.

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)

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.

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

Patients experiencing inadequate treatment on their current medication may be appropriate to **switch to or start on** a single-dose sodium oxybate with daytime symptom improvement in EDS and cataplexy.[1-3]

"What would have helped me is being asked something like: 'Some people may struggle with twice-nightly dosing, is this a challenge for you?'"—Katie, NT2

"If I had known about sodium oxybate when I was diagnosed, I would have wanted to discuss it as an option with my sleep specialist."—Wendy, NT1

SWITCH

Select the nearest equivalent dose of LUMRYZ[1]

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

OR

START

Titrate gradually based on efficacy and tolerability[1]

- Increase from recommended starting dose of 4.5 g by 1.5 g per night at weekly intervals based on efficacy and tolerability
- The recommended dosage range is 6 g to 9 g per night. Doses higher than 9 g per night have not been studied and should not ordinarily be administered

Educate your patients about a once-at-bedtime option.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (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.

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

Please see Important Safety Information throughout, and full Prescribing Information, including BOXED Warning, and Medication Guide available at LUMRYZhcp.com.

Use this survey tool to help patients verbalize their treatment experiences

What you learn from this tool can be used to discuss as a team what possible considerations may help relieve your patients' burden.

Access this survey by downloading the LUMRYZ Digital Brochure at www.lumryz.com/resources or ask your representative to leave you copies of the LUMRYZ Patient Brochure.

Read the following statements and check the boxes that apply to your experience with twice-nightly oxybates.

- ☐ I have to rely on others in my household to wake me for the second, middle-of-the-night oxybate dose
- ☐ The thought of preparing/planning the second dose of my twice-nightly oxybate treatment causes me stress and anxiety
- ☐ When I miss or mistime the second dose of my twice-nightly oxybate treatment, intentionally or accidentally, I feel the impact the following day
- ☐ My life is interrupted by my narcolepsy treatment

How often do you miss the second dose of your twice-nightly oxybate treatment (intentionally or by accident)? Circle one:

- 1-2 times per week
- 3-5 times per week
- More than 6 times per week

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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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.

ONCE AT BEDTIME

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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]
- **Removes the need** for a middle-of-the-night dose[1,5,6]
- **Premeasured packets** contain a full therapeutic dose[1]

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

RYZUP™ SUPPORT SERVICES

To get started, enroll your patient in RYZUP.
Visit **RYZUPSupport.iassist.com/single-services** or call **1-844-485-7636.**

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, including BOXED Warning, throughout and the accompanying full Prescribing Information, 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.

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