CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214755Orig1s000

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document

LUMRYZ™ (sodium oxybate extended-release) REMS Program

I. Administrative Information

Application Number: NDA 214755
Application Holder: Avadel CNS Pharmaceuticals, LLC
Initial REMS Approval: 05/2023

II. REMS Goal

The goal of the LUMRYZ REMS Program is to mitigate the risks of serious adverse outcomes resulting from inappropriate prescribing, misuse, abuse, and diversion of LUMRYZ by:

1. Informing prescribers, pharmacists, and patients of:
   a. The risk of significant central nervous system (CNS) and respiratory depression associated with LUMRYZ
   b. The contraindication of use of LUMRYZ with sedative hypnotics or alcohol
   c. The potential for abuse, misuse, and overdose associated with LUMRYZ
   d. The safe use, handling, and storage of LUMRYZ
2. Ensuring that pharmacy controls exist prior to filling prescriptions for LUMRYZ that:
   a. Screen for concomitant use of sedative hypnotics and other potentially interacting agents
   b. Monitor for inappropriate prescribing, misuse, abuse, and diversion of LUMRYZ
   c. Notify prescribers when patients are receiving concomitant contraindicated medications or there are signs of potential abuse, misuse, or diversion

III. REMS Requirements

Avadel CNS Pharmaceuticals, LLC must ensure healthcare providers, patients, pharmacies, and wholesalers, distributors, and other entities that distribute LUMRYZ comply with the following requirements:

1. Healthcare providers who prescribe LUMRYZ must:

To become certified to prescribe	1. Review the drug's Prescribing Information. 2. Review the Prescriber Brochure. 3. Enroll in the REMS by completing the Prescriber Enrollment Form and submitting it to the REMS Program.

Before treatment initiation (first dose)	4. Assess the patient's health status to determine if LUMRYZ is medically appropriate by screening for history of alcohol and drug abuse, sleep-related breathing disorders, compromised respiratory function, depression and suicidality. Document and submit to a certified pharmacy using the Prescription Form. 5. Assess the patient's health status to determine if LUMRYZ is medically appropriate by screening for concomitant use of sedative hypnotics, other CNS depressants or other potentially interacting agents. Document and submit to a certified pharmacy using the Prescription Form. 6. Counsel the patient on the serious risks and safe use, handling, and storage of LUMRYZ using the Patient Brochure. 7. Enroll the patient by completing and submitting the Patient Enrollment Form to the REMS Program. 8. Order the prescription using the Prescription Form and submit it to a certified pharmacy.
Before treatment re-initiation	9. For patients disenrolled for suspicion of abuse, misuse, or diversion: Communicate with the pharmacy regarding all relevant patient history and re-enroll the patient if the prescriber and pharmacist agree. 10. For patients with a lapse in treatment of 6 months or longer: Order the prescription using the Prescription Form and submit it to a certified pharmacy.
During treatment; within the first 3 months of starting treatment and recommended every 3 months thereafter	11. Assess the patient for concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents, serious adverse events, and signs of abuse and misuse, including an increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, and/or drug-seeking behavior.
At all times	12. Report all potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Avadel CNS Pharmaceuticals, LLC. 13. Report requests to disenroll a patient to a certified pharmacy.

2. Patients who are prescribed LUMRYZ:

Before treatment initiation	1. Review the Patient Brochure. 2. Receive counseling from the prescriber on the serious risks associated with LUMRYZ and safe use, handling, and storage of LUMRYZ using the Patient Brochure. 3. Enroll in the REMS Program by completing the Patient Enrollment Form with the prescriber. Enrollment information will be provided to the REMS Program. 4. Complete the Patient Counseling Checklist with the pharmacist.

During treatment	5. Adhere to the safe use conditions described in the Patient Brochure. 6. Complete the Patient Counseling Checklist with the pharmacist based on changes in medication and/or medical history.
During treatment; within the first 3 months of starting treatment and recommended every 3 months thereafter	7. Be monitored for concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents, serious adverse events, and signs of abuse and misuse, including an increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, and/or drug-seeking behavior.
Before treatment re-initiation, after lapse in treatment for 6 months or longer	8. Complete the Patient Counseling Checklist with the pharmacist.
At all times	9. Inform prescriber and the pharmacy about any new medications or medical conditions.

3. Pharmacies that dispense LUMRYZ must:

To become certified to dispense	1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the pharmacy. 2. Have the authorized representative review Certified Pharmacy Training Program – Pharmacy Staff Module and Pharmacist Module. 3. Have the authorized representative successfully complete the Pharmacy Staff Knowledge Assessment and Pharmacist Knowledge Assessment and submit it to the REMS Program. 4. Have the authorized representative enroll in the REMS by completing and submitting the Pharmacy Enrollment Form. 5. Train all relevant staff involved in dispensing using the Certified Pharmacy Training Program – Pharmacy Staff Module. 6. Have all relevant staff involved in dispensing successfully complete the Pharmacy Staff Knowledge Assessment. 7. Train all pharmacists involved in dispensing using the Certified Pharmacy Training Program – Pharmacy Staff Module and the Pharmacist Module. 8. Have all pharmacists involved in dispensing successfully complete the Pharmacy Staff Knowledge Assessment and Pharmacist Knowledge Assessment. 9. Establish processes and procedures to assess the patient's concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents that either are unknown to the prescriber or pose a high risk of serious interaction.

	10. Establish processes and procedures to verify and document the patient has no other active, overlapping prescriptions for sodium oxybate and other oxybate products and the patient and prescriber have not been disenrolled from any of the REMS for oxybate products for suspected abuse, misuse, or diversion by contacting the other REMS for oxybate products. 11. Establish processes and procedures to verify all prescription information including patient name and two additional identifiers, prescriber name and information, dose, titration information (if applicable), number of refills, dosing directions, total quantity (days' supply), and concomitant medications. 12. Establish processes and procedures to assess the patient's potential for abuse, misuse, and diversion by reviewing the alerts and Risk Management Report histories in the REMS Program. 13. Establish processes and procedures to provide 24/7 toll-free access to a LUMRYZ REMS trained pharmacist; to dispense no more than a one-month supply for the initial shipment and no more than a three-month supply for subsequent shipments; and to ship, track, and verify receipt of LUMRYZ to the patient or patient-authorized adult designee using an overnight service. 14. Establish processes and procedures to report each prescription filled for LUMRYZ to the other REMS for oxybate products and document to the LUMRYZ REMS Program. 15. Establish processes and procedures to reconcile LUMRYZ inventory using the pharmacy's inventory management system. 16. Establish processes and procedures to provide dispensing data and shipment and receipt dates to the REMS program.
Before dispensing	17. For new patients and existing patients who restart treatment after not receiving LUMRYZ for 6 months or longer: Counsel the patient using the Patient Counseling Checklist. Document and submit to the REMS Program using the Patient Counseling Checklist. 18. For patients who report a change in their medication use or medical history: Document and submit to the REMS Program using the Patient Counseling Checklist. 19. Assess the patient's concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents that either are unknown to the prescriber or pose a high risk of serious interaction through the processes and procedures established as a requirement of the REMS Program. 20. Verify the patient has no other active, overlapping prescriptions for oxybate products that overlap with the current prescription for LUMRYZ and that the patient and prescriber have not been disenrolled from any other REMS for oxybate products for suspected abuse, misuse, or diversion by contacting each REMS for oxybate products through the processes and procedures established as a requirement of the REMS Program. Document and submit to the REMS Program. 21. Obtain authorization by contacting the REMS Program to verify the pharmacy is certified, the prescriber is certified, the patient is enrolled, and the patient has no active, overlapping prescriptions for LUMRYZ.

	22. For patients previously disenrolled for suspicion of abuse, misuse, or diversion: Communicate all relevant patient history to the prescriber and determine whether to re-enroll the patient. 23. Verify the patient's prescription information including patient name and two additional identifiers, prescriber name and information, dose, titration information (if applicable), number of refills, dosing directions, total quantity (days' supply), and concomitant medications through the processes and procedures established as a requirement of the REMS Program. 24. Assess the patient's potential for abuse, misuse, and diversion by reviewing the alerts and Risk Management Report histories in the REMS Program. 25. For patients who request an early refill or if abuse, misuse or diversion is suspected: Discuss the request or concern with the prescriber. 26. Dispense no more than a one-month (30 day) supply for the initial shipment. 27. Dispense no more than a three-month (90 day) supply for subsequent shipments.
Before shipping	28. Verify the patient's shipping address and that the patient or patient-authorized adult designee will be available to receive the shipment through the processes and procedures established as a requirement of the REMS. 29. Ship LUMRYZ directly to each patient or a patient-authorized adult designee through the processes and procedures established as a requirement of the REMS. 30. Provide new patients with the Patient Brochure with their first shipment.
After shipping	31. Track and verify receipt of each shipment of LUMRYZ through the processes and procedures established as a requirement of the REMS. 32. Document and submit the dispensing data, and shipment and receipt dates to the REMS Program.
To maintain certification to dispense, every year	33. Train all relevant staff involved in dispensing LUMRYZ using the Certified Pharmacy Training Program – Pharmacy Staff Module. 34. Have all pharmacy staff involved in dispensing LUMRYZ successfully complete the Pharmacy Staff Knowledge Assessment. 35. Train all pharmacists involved in dispensing LUMRYZ using the Certified Pharmacy Training Program – Pharmacy Staff Module and Pharmacist Module. 36. Have all pharmacists involved in dispensing LUMRYZ successfully complete the Pharmacy Staff Knowledge Assessment and Pharmacist Knowledge Assessment.
At all times	37. Provide 24/7 toll-free access to a REMS trained pharmacist. 38. Ship LUMRYZ directly to the patient or a patient-authorized adult designee using an overnight service. 39. Document and report all potential adverse events reported by all sources, including CNS depression, respiratory depression, loss of consciousness, coma, and death to Avadel CNS Pharmaceuticals, LLC.

40. Report lost, stolen, destroyed, or spilled drug to the REMS Program using the Risk Management Report.

41. Report each prescription filled for LUMRYZ to each REMS for oxybate products through the processes and procedures established as a requirement of the REMS. Document and submit to the REMS Program.

42. Monitor all instances of patient and prescriber behavior that give rise to a reasonable suspicion of abuse, misuse, and diversion, including all requests for early refills, and all reports of lost, stolen, destroyed, or spilled drug. Report to the REMS Program by completing and submitting a Risk Management Report.

43. Not distribute, transfer, loan, or sell LUMRYZ.

44. Not stock LUMRYZ in retail pharmacies.

45. Maintain records of staff training and completion of knowledge assessments.

46. Maintain records of inventory reconciliation using the pharmacy's inventory management system.

47. Maintain records of all processes and procedures including compliance with those processes and procedures.

48. Comply with audits carried out by Avadel CNS Pharmaceuticals, LLC or a third party acting on behalf of Avadel CNS Pharmaceuticals, LLC to ensure all processes and procedures are in place and are being followed.

Wholesalers, distributors, and other entities that distribute LUMRYZ must:

To be able to distribute	1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies. 2. Train all relevant staff involved in distributing LUMRYZ on the program requirements.
At all times	3. Distribute only to certified pharmacies. 4. Maintain records of all drug distributions. 5. Comply with audits carried out by Avadel CNS Pharmaceuticals, LLC or a third party acting on behalf of Avadel CNS Pharmaceuticals, LLC to ensure all processes and procedures are in place and are being followed.

Avadel CNS Pharmaceuticals, LLC must provide training to healthcare providers who prescribe LUMRYZ.
The training includes the following educational material: Prescriber Brochure. The training must be available on the REMS Program website or delivered by Avadel CNS Pharmaceuticals, LLC.

Avadel CNS Pharmaceuticals, LLC must provide training to the pharmacies that dispense LUMRYZ.
The training includes the following educational materials: Certified Pharmacy Training Program – Pharmacy Staff Module and Pharmacist Module, Pharmacy Staff Knowledge Assessment, and Pharmacist Knowledge Assessment. The training must be available on the REMS Program website or delivered by Avadel CNS Pharmaceuticals, LLC.

To inform healthcare providers about the REMS Program and the risks and safe use of LUMRYZ, Avadel CNS Pharmaceuticals, LLC must disseminate REMS communication materials according to the table below:

Target Audience	Communication Materials & Dissemination Plans
Healthcare providers who are likely to prescribe LUMRYZ	REMS Letters: Healthcare Provider REMS Letter, Professional Society REMS Letter, with attachments LUMRYZ Prescribing Information, Fact Sheet 1. Email within 14 calendar days of the date LUMRYZ is first commercially distributed and 30 calendar days later. a. Send by mail within 30 calendar days of the date the first email was sent if a healthcare provider's email address is not available or the email is undeliverable. b. Send a second email within 30 calendar days of the date the first email was sent if the first email is marked as unopened. c. Send by mail within 30 calendar days of the date the second email was sent if the second email is marked as unopened. 2. Disseminate through the following professional societies and request the letter or content be provided to their members: a. American Academy of Neurology, American College of Chest Physicians, Academy American of Sleep Medicine, National Institute of Neurological Disorders and Stroke, National Organization for Rare Disorders, American Psychiatric Association, Society of General Internal Medicine, American College of Physicians – Internal Medicine Society, American Academy of Family Physicians, American Academy of Physician Assistants, and American Association of Nurse Practitioners.

To support REMS Program operations, Avadel CNS Pharmaceuticals, LLC must:

1. Not stock LUMRYZ in retail pharmacies.

2. Authorize dispensing for each patient after verifying the pharmacy is certified, the prescriber is certified, the patient is enrolled, and the patient has no active, overlapping prescriptions for LUMRYZ or another oxybate product.

3. Establish and maintain a REMS Program website: www.LUMRYZREMS.com. The REMS Program website must include the capability to complete prescriber certification online, complete pharmacy staff and pharmacist knowledge assessments, the capability to enroll and manage patients online, including the capability for pharmacies to obtain an authorization to dispense, complete Risk Management Reports, complete the Patient Counseling Checklist, and the option to print the Prescribing Information, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website. The REMS Program website must not link to promotional product website(s).

4. Make the REMS Program website fully operational and all REMS materials available through the REMS Program website and call center by the date LUMRYZ is first commercially distributed.

5. Establish and maintain a REMS Program call center for REMS participants at 1-877-453-1029.

6. Establish and maintain validated, secure, separate and distinct databases of all REMS participants enrolled, certified and/or disenrolled in the REMS Program, including a patient database, certified prescriber database, certified pharmacy database, and disenrolled prescriber database that will be queried independently through electronic verification.

7. Ensure prescribers are able to submit the Prescriber Enrollment Form online and by fax.

8. Ensure prescribers are able to submit the Patient Enrollment Form online and by fax.

9. Ensure prescribers are able to submit the Prescription Form by fax and mail.

10. Ensure prescribers are able to add refills and renew prescriptions by phone, fax, mail, and online through a prescribing system.

11. Ensure patients are able to change certified prescribers.

12. Ensure pharmacies are able to submit the Pharmacy Enrollment Form by fax.

13. Ensure pharmacies are able to obtain authorization to dispense LUMRYZ online, including through the pharmacy's pharmacy management system, and by phone.

14. Ensure pharmacies are able to report lost, stolen, destroyed or spilled LUMRYZ by completing and submitting a Risk Management Report online and by fax.

15. Ensure pharmacies are able to verify by phone the patient has no other active, overlapping prescriptions for oxybate products and that the patient and prescriber have not been disenrolled from the other REMS for oxybate products for suspected abuse, misuse, or diversion.

16. Ensure pharmacies are able to create an alert in the patient's profile for repeated incidents of lost, stolen, destroyed, or spilled drug by completing and submitting a Risk Management Report online and by fax.

17. Ensure pharmacies and prescribers are able to request to disenroll a patient after review or receiving report of incidents suggestive of abuse, misuse, or diversion by completing and submitting a Risk Management Report online and by fax.

18. Ensure pharmacies are able to request to disenroll a prescriber by completing and submitting a Risk Management Report online and by fax.

19. Report patient and prescriber disenrollment in the LUMRYZ REMS Program due to suspected abuse, misuse, or diversion to other REMS for oxybate products by phone. Document in the LUMRYZ REMS Program databases.

20. Notify prescribers within two (2) business days after they become certified in the REMS Program.

21. Provide certified pharmacies access to the REMS Program databases of enrolled and disenrolled patients.

To ensure REMS participants' compliance with the REMS Program, Avadel CNS Pharmaceuticals, LLC must:

22. Verify annually that the authorized representative's name and contact information correspond to those of the current designated authorized representative for the pharmacy. If different, the pharmacy must be required to re-certify with a new authorized representative.

23. Maintain adequate records to demonstrate REMS requirements have been met, including, but not limited to, records of: LUMRYZ distribution and dispensing; certification of prescribers and pharmacies; enrolled patients; and audits of REMS participants. These records must be readily available for FDA inspections.

24. Establish a plan for addressing noncompliance with REMS Program requirements.

25. Monitor prescribers and pharmacies on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if noncompliance is identified, including de-certification.

26. Monitor certified prescribers and pharmacies for timely reporting to Avadel CNS Pharmaceuticals, LLC of all potential adverse events and any behavior by patients or prescribers enrolled in the REMS Program that raises suspicion of abuse, misuse, or diversion.

27. Audit certified pharmacies within 90 calendar days after the pharmacy places its first order of LUMRYZ, and annually thereafter, to ensure all REMS processes and procedures are in place, functioning, and comply with REMS Program requirements.

28. Audit wholesalers, distributors, and other entities that distribute LUMRYZ within 90 calendar days after LUMRYZ is first commercially distributed and annually thereafter to ensure all REMS processes and procedures are in place, functioning, and comply with REMS Program requirements.

29. Take reasonable steps to improve implementation of and compliance with the requirements in the REMS Program based on monitoring and evaluation of the REMS Program.

IV. REMS Assessment Timetable

Avadel CNS Pharmaceuticals, LLC must submit REMS Assessments at 6 months, 12 months, and annually thereafter from the date of the initial approval of the REMS (05/01/2023). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Avadel CNS Pharmaceuticals, LLC must submit each assessment so it will be received by FDA on or before the due date.

V. REMS Materials

The following materials are part of the LUMRYZ REMS:

Enrollment Forms:

Prescriber:

1. Prescriber Enrollment Form

Patient:

2. Patient Enrollment Form

Pharmacy:

3. Pharmacy Enrollment Form

Training and Educational Materials:

Prescriber:

4. Prescriber Brochure

Patient:

5. Patient Brochure

Pharmacy:

6. Certified Pharmacy Training Program

7. Pharmacy Staff Knowledge Assessment

8. Pharmacist Knowledge Assessment

Patient Care Forms:

9. Prescription Form

10. Patient Counseling Checklist

Communication Materials:

11. Dear Healthcare Provider Letter

12. Dear Professional Society Letter

13. REMS Fact Sheet

Other Materials:

14. Risk Management Report

15. REMS Program Website

LUMRYZ™ REMS | Prescriber Enrollment Form

Lumryz
(sodium oxybate) for extended-release oral suspension

Complete and submit this form online at www.LUMRYZREMS.com, OR fax to 1-877-206-3198 (toll free).

For more information, please call the LUMRYZ REMS at 1-877-453-1029.

TO BECOME A CERTIFIED PRESCRIBER IN THE LUMRYZ REMS AND PRESCRIBE LUMRYZ:

1. Review the LUMRYZ Prescribing Information.
2. Review the *Prescriber Brochure*.
3. Complete steps 1, 2 and 3 below and submit this *Prescriber Enrollment Form* to the LUMRYZ REMS.

STEP 1: PRESCRIBER ATTESTATIONS

I have:
- Reviewed the Prescribing Information.
- Reviewed the *Prescriber Brochure*.

I understand:
- LUMRYZ is approved for the treatment of
  - Cataplexy in adults with narcolepsy.
  - Excessive daytime sleepiness (EDS) in adults with narcolepsy.
- LUMRYZ is a Schedule III central nervous system (CNS) depressant and can cause obtundation and clinically significant respiratory depression at recommended doses.
- LUMRYZ is contraindicated in combination with alcohol and sedative hypnotics.
- Concurrent use of LUMRYZ with certain other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptic drugs, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death.
- Patients who have sleep apnea or compromised respiratory function (e.g., asthma, COPD, etc.) may be at higher risk of developing respiratory depression, loss of consciousness, coma, and death with LUMRYZ use.

Before treatment initiation (first dose), I must:
- Screen for history of alcohol and drug abuse, sleep-related breathing disorders, compromised respiratory function, depression, suicidality, concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents. Document my findings on the *Prescription Form*.
- Counsel the patient on the serious risks and safe use, handling, and storage of LUMRYZ using the *Patient Brochure*.
- Enroll the patient by completing and submitting the *Patient Enrollment Form* to the REMS.
- Order LUMRYZ using the *Prescription Form* and submit it to a certified pharmacy.

Before treatment re-initiation, I must:
- **For patients disenrolled for suspicion of abuse, misuse, or diversion:** Communicate with the pharmacy regarding all relevant patient history and re-enroll the patient if the pharmacist and I agree.
- **For patients with a lapse in treatment of 6 months or longer:** Order LUMRYZ using the *Prescription Form* and submit it to a certified pharmacy.

Within the first 3 months of starting treatment, I must:
- Assess the patient for concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents, serious adverse events, and signs of abuse and misuse, including an increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, and/or drug-seeking behavior.

It is recommended that patients be re-assessed every 3 months while taking LUMRYZ.

I must:
- Report potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Avadel CNS Pharmaceuticals, LLC.
- Report requests to disenroll a patient to a certified pharmacy.

STEP 2: TO HELP EXPEDITE THE ENROLLMENT PROCESS, PLEASE COMPLETE ALL REQUIRED FIELDS (PLEASE PRINT)

PRESCRIBER INFORMATION

(*denotes required field)

*First Name:	M.I.:	*Last Name:	*DEA No.:

Facility/Practice Name:	*State License No.:	*NPI No.:

*Professional Designation: ☐ MD ☐ DO ☐ PA ☐ NP ☐ Other _____

*Medical Specialty: ☐ Sleep Medicine ☐ Neurology ☐ Pulmonology ☐ Psychiatry ☐ Internal Medicine ☐ Other _____

*Address Line 1:

Address Line 2:

*City:	*State:	*Zip Code:

*Phone:	*Fax:	*Email:

*Preferred Method of Contact: ☐ Email ☐ Fax

Office Contact First Name:	Office Contact Last Name:	Office Contact Phone:

STEP 3: PRESCRIBER SIGNATURE IS REQUIRED BELOW FOR ENROLLMENT IN THE LUMRYZ REMS

By signing below, I acknowledge the above attestations, and I understand my personally identifiable information provided above will be shared with Avadel CNS Pharmaceuticals, LLC, its agents, contractors, and affiliates and entered into a prescriber database for the LUMRYZ REMS. I agree that I may be contacted in the future by mail, email, fax, and/or telephone concerning LUMRYZ, the LUMRYZ REMS, and other LUMRYZ programs and services.

_____ *Prescriber Signature

_____ *Date

Report adverse events to Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335.

Avadel

Reference ID: 5166429

LUMRYZ™ REMS | Patient Enrollment Form

Lumryz
(sodium oxybate) for extended-release oral suspension

Complete and submit this form online at www.LUMRYZREMS.com, OR fax to 1-877-206-3198 (toll free).

For more information, please call the LUMRYZ REMS at 1-877-453-1029.

In order to receive LUMRYZ, patients must be enrolled in the LUMRYZ REMS. To enroll a patient, the prescriber and the patient must complete, sign and submit this form to the LUMRYZ REMS.

To help expedite the enrollment process, please complete all required fields - please print (*denotes required field)

PATIENT INFORMATION

*First Name:	M.I.:	*Last Name:	*Primary Phone:
*Date of Birth (MM/DD/YYYY):	*Gender (select one): ☐ Male ☐ Female ☐ Other		Cell Phone:
*Address Line 1:			Work Phone:
Address Line 2:			
*City:	*State:	*Zip Code:	*Email:

Is patient currently or has patient ever been enrolled in an oxybate product REMS? ☐ Yes ☐ No

PRESCRIBER INFORMATION

*First Name:	*Last Name:
*Phone:	*NPI No.:

PATIENT ATTESTATIONS:

Before I start treatment, I must:

- Review the *Patient Brochure*
- Receive counseling from my doctor/prescriber about the serious risks with LUMRYZ and the safe use, handling, and storage of LUMRYZ
- Enroll in the REMS by completing the *Patient Enrollment Form* with my prescriber
- Complete the *Patient Counseling Checklist* with the pharmacist

During treatment

- Follow the safe use instructions explained to me by my doctor/prescriber
- Tell my pharmacist about any changes in the medicines I am taking and any changes in my medical history so I can be monitored for problems with the medicines I'm taking and signs of abuse and misuse of LUMRYZ

At all times

- I understand that my personally identifiable information provided above will be shared with the LUMRYZ REMS, its agents, contractors, and affiliates, and entered into a patient database for the LUMRYZ REMS
- I understand that my personally identifiable information provided above may be shared with other REMS for oxybate salt medicines, their agents, contractors, and affiliates
- I agree that Avadel CNS Pharmaceuticals, LLC and its agents may contact me or my doctor/prescriber via phone, mail, or email to support administration of the LUMRYZ REMS
- I agree to inform my doctor/prescriber and pharmacy about changes in my medication use or medical history

_____ *Pa ient/Guardian Signature

_____ *Date

* Printed Guardian Name, if applicable: First Name: _____ Last Name: _____

PRESCRIBER:

By signing below, I acknowledge that:

- I have counseled the patient about the serious risks associated with the use of LUMRYZ and the safe use conditions as described in the *Patient Brochure*
- I have provided the patient with the *Patient Brochure* (optional)

_____ *Prescriber Signature

_____ *Date

LUMRYZ™ REMS | Pharmacy Enrollment Form

Lumryz.
(sodium oxybate) for extended-release oral suspension C

Pharmacies must be certified in the LUMRYZ REMS to dispense LUMRYZ. To become certified, every pharmacy must designate an authorized representative to:

1. Complete certification using this *Pharmacy Enrollment Form* and fax the completed form to the LUMRYZ REMS at 1-877-206-3198.
2. Review the *Certified Pharmacy Training Program* and submit the completed *Pharmacy Staff Knowledge Assessment* and *Pharmacist Knowledge Assessment* online at www.LUMRYZREMS.com or by fax to 1-877-206-3198.
3. Provide relevant training to the pharmacy staff and pharmacists in each pharmacy and maintain a record of the training.
4. Ensure the pharmacy enables its Pharmacy Management System (PMS) to support electronic communication with the LUMRYZ REMS system using established telecommunication standards.

AUTHORIZED REPRESENTATIVE RESPONSIBILITIES

As the authorized representative, I must:

- Review the *Certified Pharmacy Training Program – Pharmacy Staff Module* and *Pharmacist Module*.
- Successfully complete the *Pharmacy Staff Knowledge Assessment* and *Pharmacist Knowledge Assessment* and submit it to the REMS.
- Complete and submit the *Pharmacy Enrollment Form*.
- Train all relevant staff involved in dispensing using the *Certified Pharmacy Training Program – Pharmacy Staff Module*.
- Have all relevant staff involved in dispensing successfully complete the *Pharmacy Staff Knowledge Assessment*.
- Train all pharmacists involved in dispensing using the *Certified Pharmacy Training Program – Pharmacy Staff Module* and the *Pharmacist Module*.
- Have all pharmacists involved in dispensing successfully complete the *Pharmacy Staff Knowledge Assessment* and *Pharmacist Knowledge Assessment*.
- Establish processes and procedures to assess the patient's concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents that either are unknown to the prescriber or pose a high risk of serious interaction.
- Establish processes and procedures to verify and document the patient has no other active, overlapping prescriptions for sodium oxybate and other oxybate products and the patient and prescriber have not been disenrolled from any of the REMS for oxybate products for suspected abuse, misuse, or diversion by contacting the other REMS for oxybate products.
- Establish processes and procedures to verify all prescription information including patient name and two additional identifiers, prescriber name and information, dose, titration information (if applicable), number of refills, dosing directions, total quantity (days' supply), and concomitant medications.
- Establish processes and procedures to assess the patient's potential for abuse, misuse, and diversion by reviewing the alerts and *Risk Management Report* histories in the REMS.
- Establish processes and procedures to provide 24/7 toll-free access to a LUMRYZ REMS trained pharmacist; to dispense no more than a one-month supply for the initial shipment and no more than a three-month supply for subsequent shipments; and to ship, track, and verify receipt of LUMRYZ to the patient or patient-authorized adult designee using an overnight service.
- Establish processes and procedures to report each prescription filled for LUMRYZ to the other REMS for oxybate products and document to the LUMRYZ REMS.
- Establish processes and procedures to reconcile LUMRYZ inventory using the pharmacy's inventory management system.
- Establish processes and procedures to provide dispensing data and shipment and receipt dates to the REMS.
- Not stock LUMRYZ in retail pharmacies.
- Maintain records of staff training and completion of knowledge assessments.
- Maintain records of inventory reconciliation using the pharmacy's inventory management system.
- Maintain records of all processes and procedures including compliance with those processes and procedures.
- Comply with audits carried out by Avadel CNS Pharmaceuticals, LLC or a third party acting on behalf of Avadel CNS Pharmaceuticals, LLC to ensure all processes and procedures are in place and are being followed.

Before dispensing, all pharmacy staff must:

- For new patients and existing patients who restart treatment after not receiving LUMRYZ for 6 months or longer: Counsel the patient using the *Patient Counseling Checklist*. Document and submit to the REMS using the *Patient Counseling Checklist*.
- For patients who report a change in their medication use or medical history: Document and submit to the REMS using the *Patient Counseling Checklist*.
- Assess the patient's concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents either are unknown to the prescriber or pose a high risk of serious interaction through the processes and procedures established as a requirement of the REMS.
- Verify the patient has no other active, overlapping prescriptions for oxybate products that overlaps with the current prescription for LUMRYZ and that the patient and prescriber have not been disenrolled from the other REMS for oxybate products for suspected abuse, misuse, or diversion by contacting each REMS for oxybate products through the processes and procedures established as a requirement of the REMS. Document and submit to the REMS.
- Obtain authorization by contacting the REMS to verify the pharmacy is certified, the prescriber is certified, the patient is enrolled, and the patient has no active, overlapping prescriptions for LUMRYZ.
- For patients previously disenrolled for suspicion of abuse, misuse, or diversion: Communicate all relevant patient history to the prescriber and determine whether to re-enroll the patient.
- Verify the patient's prescription information including patient name and two additional identifiers, prescriber name and information, dose, titration information (if applicable), number of refills, dosing directions, total quantity (days' supply), and concomitant medications through the processes and procedures established as a requirement of the REMS.
- Assess the patient's potential for abuse, misuse, and diversion by reviewing the alerts and Risk Management Report histories in the REMS.
- For patients who request an early refill or if abuse, misuse or diversion is suspected: Discuss the request or concern with the prescriber.
- Dispense no more than a one-month (30 day) supply for the initial shipment.
- Dispense no more than a three-month (90 day) supply for subsequent shipments.

Before shipping, all pharmacy staff must:

- Verify the patient's shipping address and that the patient or patient-authorized adult designee will be available to receive the shipment through the processes and procedures established as a requirement of the REMS.
- Ship LUMRYZ directly to each patient or a patient-authorized adult designee through the processes and procedures established as a requirement of the REMS.
- Provide new patients with the *Patient Brochure* with their first shipment.

CONTINUED >>

Lumryz.
(sodium oxybate) for extended-release oral suspension ℂ

After shipping, all pharmacy staff must:

- Track and verify receipt of each shipment of LUMRYZ through the processes and procedures established as a requirement of the REMS.
- Document and submit the dispensing data, and shipment and receipt dates to the REMS.

All pharmacy staff must:

- Ship LUMRYZ directly to the patient or a patient-authorized adult designee using an overnight service.
- Document and report all potential adverse events reported by all sources, including CNS depression, respiratory depression, loss of consciousness, coma, and death to Avadel CNS Pharmaceuticals, LLC.
- Report lost, stolen, destroyed, or spilled drug to the REMS using the *Risk Management Report*.
- Report each prescription filled for LUMRYZ to each REMS for oxybate products through the processes and procedures established as a requirement of the REMS. Document and submit to the REMS.
- Monitor all instances of patient and prescriber behavior that give rise to a reasonable suspicion of abuse, misuse, and diversion, including all requests for early refills, and all reports of lost, stolen, destroyed, or spilled drug. Report to the REMS by completing and submitting a *Risk Management Report*.
- Not distribute, transfer, loan, or sell LUMRYZ.

To maintain certification to dispense LUMRYZ, every year the authorized representative must:

- Train all relevant staff involved in dispensing LUMRYZ using the *Certified Pharmacy Training Program – Pharmacy Staff Module*.
- Have all pharmacy staff involved in dispensing LUMRYZ successfully complete the *Pharmacy Staff Knowledge Assessment*.
- Train all pharmacists involved in dispensing LUMRYZ using the *Certified Pharmacy Training Program – Pharmacy Staff Module* and *Pharmacist Module*.
- Have all pharmacists involved in dispensing LUMRYZ successfully complete the *Pharmacy Staff Knowledge Assessment* and *Pharmacist Knowledge Assessment*.

PHARMACY INFORMATION

(*denotes required field)

*Pharmacy Name:		
*Address Line 1:		
Address Line 2:		
*City:	*State:	*Zip Code:
NCPDP No.:	*NPI No.:	*DEA No.:

AUTHORIZED REPRESENTATIVE INFORMATION

(All fields required)

First Name:	Last Name:	
Phone:	Fax:	Email:
Preferred Contact Method: ☐ Phone ☐ Fax ☐ Email		

_____
*Authorized Representative Signature

_____
*Date

LUMRYZ™ REMS

PRESCRIBER BROCHURE

Lumryz™

(sodium oxybate) for extended-release oral suspension Ⓒ

Reference ID: 5166429

Lumryz.

(sodium oxybate) for extended-release oral suspension

Dear Prescriber,

The LUMRYZ REMS was developed in collaboration with the Food and Drug Administration (FDA) as a Risk Evaluation and Mitigation Strategy (REMS). A REMS is a strategy to manage known or potential serious risks associated with a drug product and is required by the FDA to ensure the benefits of a drug outweigh its risks.

This brochure provides valuable information about the LUMRYZ REMS that includes important prescribing information, educational and counseling requirements, and materials necessary for REMS enrollment and prescribing LUMRYZ (sodium oxybate) for extended-release oral suspension, including:

- *Prescriber Enrollment Form*—a one-time enrollment is required for all prescribers of LUMRYZ.
- *Patient Enrollment Form*—a one-time patient enrollment in the LUMRYZ REMS is required for each new patient for whom LUMRYZ will be prescribed.
- *Prescription Form*—This form must be used for new prescriptions and may also be used for refills and renewals of LUMRYZ prescriptions.
- *Patient Brochure*—answers important questions for adult patients about how to obtain LUMRYZ, how to use LUMRYZ properly, and how to store it safely. It also gives important information about the risks associated with LUMRYZ.

Healthcare providers who prescribe LUMRYZ must be certified in the LUMRYZ REMS. The *Prescriber Enrollment Form* and *Patient Enrollment Form* must be completed in full and sent to the LUMRYZ REMS. The *Prescription Form* must be completed in full and sent to a certified pharmacy. For your convenience, the *Prescriber Enrollment Form, Patient Enrollment Form,* and *Prescription Form* are available online at www.LUMRYZREMS.com. All forms can be requested by calling the LUMRYZ REMS toll-free at 1-877-453-1029. Only pharmacies certified in the REMS can process LUMRYZ prescriptions. A list of certified pharmacies is available in the secure certified prescriber website portal at www.LUMRYZREMS.com or by calling the LUMRYZ REMS.

Continue reading this brochure to learn more about the LUMRYZ REMS and your responsibilities as a prescriber of LUMRYZ. Please review the Prescribing Information for LUMRYZ.

LUMRYZ may be dispensed only to patients enrolled in the LUMRYZ REMS.

LUMRYZ is approved for the treatment of:

- **Cataplexy in adults with narcolepsy**
- **Excessive daytime sleepiness (EDS) in adults with narcolepsy**

If you require any additional assistance or information, please call the LUMRYZ REMS at 1-877-453-1029 or visit www.LUMRYZREMS.com.

Sincerely,

Avadel CNS Pharmaceuticals, LLC

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

LUMRYZ is contraindicated for use in:

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

WARNINGS AND PRECAUTIONS

Central Nervous System Depression

- LUMRYZ is a central nervous system (CNS) depressant. 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.
  - If short-term use of an opioid (e.g., post- or perioperative) is required, interruption of treatment with LUMRYZ should be considered.
- Patients who have sleep apnea or compromised respiratory function may be at a higher risk of developing respiratory depression, loss of consciousness, coma, and death with LUMRYZ use.
- Healthcare providers should caution patients about operating hazardous machinery, including automobiles or airplanes, until they are reasonably certain that LUMRYZ does not affect them adversely (e.g., impaired judgment, thinking, or motor skills). Patients should not engage in hazardous occupations or activities requiring complete mental alertness or motor coordination, such as operating machinery or a motor vehicle or flying an airplane, for at least 6 hours after taking LUMRYZ.

Abuse and Misuse

- LUMRYZ is a Schedule III controlled substance.
- The active ingredient in 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 (e.g., assault victim).
- You should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of GHB (e.g., increase in size or frequency of dosing; reports of lost, stolen, or spilled medication; drug-seeking behavior; feigned cataplexy).

LUMRYZ REMS

- LUMRYZ is to be prescribed only to patients enrolled in the 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. To be certified, prescribers must complete the *Prescriber Enrollment Form* and comply with the LUMRYZ REMS requirements.
  - 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. To be enrolled, patients must sign the *Patient Enrollment Form* and acknowledge that they have been counseled on the serious risks and safe use of LUMRYZ.

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

Depression, Suicidality, and Other Behavioral / Psychiatric Adverse Reactions

- Depression, suicidal ideation and behavior, and other behavioral and psychiatric adverse reactions can occur in patients taking LUMRYZ.
- 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 suicide attempt should be monitored carefully for the emergence of depressive symptoms while taking LUMRYZ. Psychiatric reactions reported in adult clinical trials in patients with narcolepsy administered LUMRYZ included irritability, emotional disorder, panic attack, agitation, delirium, and obsessive thoughts. Patients should be instructed to call their healthcare provider if they experience any of these events.
- Anxiety can also occur in patients treated with LUMRYZ.

Use in Patients Sensitive to High Sodium Intake

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

Most Common Adverse Events

- In the placebo-controlled clinical trial for LUMRYZ, the most common adverse reactions reported for any dose of LUMRYZ were nausea, dizziness, enuresis, headache, and vomiting.

Adverse Reactions Leading to Treatment Discontinuation

- In Study 1, 15.9% of patients treated with LUMRYZ discontinued because of adverse reactions compared to 1.9% of patients receiving placebo. The most common adverse reaction leading to discontinuation was dizziness (4.7%). For LUMRYZ, 5.6% of patients discontinued due to adverse reactions on 4.5 g, 4.1% on the 6 g, 4.5% on the 7.5 g, and 3.9% on 9 g dose.

TABLE OF CONTENTS

Prescribing Information is also included.

Reference ID: 5166429

PRESCRIBING LUMRYZ—A BRIEF GUIDE

The procedure for writing and dispensing prescriptions for LUMRYZ is outlined below.

PRESCRIBERS OF LUMRYZ

Prescribing LUMRYZ requires a one-time enrollment.

- If you are prescribing LUMRYZ for the first time, complete the *Prescriber Enrollment Form*, found either accompanying this *Prescriber Brochure* or online at www.LUMRYZREMS.com. Please:
  - Submit the form online at www.LUMRYZREMS.com, or
  - Fax to 1-877-206-3198
- On the *Prescriber Enrollment Form*, please confirm that:
  - You understand LUMRYZ is approved for:
    - Treatment of cataplexy in adults with narcolepsy
    - Treatment of excessive daytime sleepiness (EDS) in adults with narcolepsy
  - You have read and understand the Prescribing Information and this *Prescriber Brochure*

SCREEN

- You agree to screen each patient for the following and document and submit to a certified pharmacy using the *Prescription Form:*
  - History of alcohol and drug abuse
  - History of sleep-related breathing disorders
  - History of compromised respiratory function
  - Concomitant use of sedative hypnotics, other CNS depressants or other potentially interacting agents
  - History of depression and suicidality

COUNSEL

- You agree to counsel your patients on:
  - The serious risks associated with LUMRYZ
  - Contraindications (alcohol and sedative hypnotics)
  - Risks of concomitant use of LUMRYZ with alcohol and/or certain other CNS depressants
  - Risk of operating hazardous machinery, including automobiles or airplanes, for at least 6 hours after taking LUMRYZ
  - Preparation and dosing instructions for LUMRYZ
  - Risk of abuse and misuse associated with use of LUMRYZ
  - Safe use, handling, and storage of LUMRYZ

ENROLL

- You will enroll each patient in the LUMRYZ REMS by completing the one-time *Patient Enrollment Form* and submitting the form to the LUMRYZ REMS.
- You will evaluate each patient within the first 3 months of starting LUMRYZ, including an evaluation of the following. It is recommended that patients be reevaluated every 3 months thereafter while on LUMRYZ therapy:
  - Concomitant use of sedative hypnotics, other CNS depressants or other potentially interacting agents
  - Serious adverse events
  - Signs of abuse, misuse, and diversion, such as an increase in dose or frequency of dosing; reports of lost, stolen, or spilled medication; and/or drug-seeking behavior

REPORT

- You will report all potential serious adverse events including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335.
- Report requests to disenroll a patient to a certified pharmacy

Reference ID: 5166429

PATIENT ENROLLMENT

All patients must be enrolled one time in the LUMRYZ REMS.

- On the *Patient Enrollment Form*, please:
  - Verify you have provided counseling to the patient about the serious risks associated with the use of LUMRYZ and the safe use conditions as described in the *Patient Brochure*.
  - Obtain a mandatory patient or guardian signature acknowledging the patient i) has been counseled on the serious risks and safe use conditions of LUMRYZ, ii) has had the opportunity to ask you any questions he/she may have about LUMRYZ, iii) grants you the authority to release personal information to the LUMRYZ REMS, other REMS for oxybate products, and partners and agents of the LUMRYZ REMS, including the certified pharmacy that will fill the prescription, and iv) agree that Avadel CNS Pharmaceuticals, LLC and agents may contact him/her to support administration of the REMS.
- Complete the *Patient Enrollment Form* online at www.LUMRYZREMS.com or fax the completed form to the LUMRYZ REMS at 1-877-206-3198.

PRESCRIBING REQUIREMENTS

Write prescriptions for both new and existing patients using the *Prescription Form* and submit them to a LUMRYZ REMS certified pharmacy. If the patient has a lapse in therapy for 6 months or more, a new prescription will be required.

- Fill out the *Prescription Form* completely and clearly to ensure timely fulfillment of your patient's prescription.

Verify that you have screened your patient for:

- History of alcohol or substance abuse
- History of sleep-related breathing disorders
- History of compromised respiratory function
- Concomitant use of sedative hypnotics, other CNS depressants or other potentially interacting agents
- History of depression or suicidality

Verify that you have counseled the patient regarding:

- The serious risks associated with LUMRYZ
- Contraindications (alcohol or sedative hypnotics)
- Risk of concomitant use of LUMRYZ with alcohol and/or certain other CNS depressants
- Preparation and dosing instructions for LUMRYZ
- Risk of abuse and misuse associated with use of LUMRYZ
- Risk of operating hazardous machinery, including automobiles or airplanes, for at least 6 hours after taking a dose of LUMRYZ
- Safe use, handling, and storage of LUMRYZ

Provide a list of all current prescription and non-prescription medications and dosages that the patient is currently taking to the best of your knowledge. Additionally, indicate the presence of relevant comorbid medical conditions.

NOTE: Prior to dispensing each LUMRYZ prescription (including refills), the certified pharmacy responsible for dispensing LUMRYZ to the patient will complete the patient counseling process and will ask the patient about the use of other medicines. If the patient's certified pharmacy learns the patient has a previous undisclosed comorbid condition or is taking a previously undisclosed contraindicated medication (sedative hypnotics), an opioid, more than one CNS depressant, or other potentially interacting agent and the prescriber has not indicated awareness of the comorbid condition or concomitant medication, the patient's certified pharmacy will contact and inform the prescriber of the comorbid condition or concomitant medication use prior to dispensing LUMRYZ. The patient's certified pharmacy may also contact the prescriber about other concomitant medications of concern.

- Verify you have informed the patient that his/her certified pharmacy will send him/her a copy of the *Patient Brochure* with his/her first LUMRYZ prescription fill. This material is available through the LUMRYZ REMS at www.LUMRYZREMS.com.
- Access the secure certified prescriber website portal at www.LUMRYZREMS.com to look up the certified pharmacies.
- Fax the completed *Prescription Form* and all renewal/refill prescriptions to a certified pharmacy.

PATIENT EVALUATION

- Evaluate each patient within the first 3 months of starting LUMRYZ therapy, including an evaluation of the following. It is recommended that patients be re-evaluated every 3 months thereafter while they are taking LUMRYZ.
  - Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents
  - Serious adverse events
  - Signs of abuse, misuse, and diversion, such as an increase in dose or frequency of dosing; reports of lost, stolen, or spilled medication; and/or drug-seeking behavior
- At all times
  - Report requests to disenroll a patient to a certified pharmacy

REFILL PRESCRIPTIONS

- Up to 5 refills are allowed on a LUMRYZ prescription (per DEA regulations for Schedule lll controlled substances).
- Prescription refills and renewals may be conveyed by phone, fax, mail, and online through a prescribing system to the patient's certified pharmacy. The patient's certified pharmacy will send you a *Prescription Form* upon request.
  - Fill out the *Prescription Form* completely and clearly to ensure timely fulfillment of your patient's prescription.
  - Access www.LUMRYZREMS.com to look up the certified pharmacies.
  - Fax the completed *Prescription Form* and all subsequent prescriptions to a certified pharmacy.

Responsibilities of the LUMRYZ REMS Certified Pharmacy

FOLLOWING RECEIPT OF A PATIENT'S PRESCRIPTION THE CERTIFIED PHARMACY WILL:

- Provide you with confirmation of each new LUMRYZ prescription received from your office
- Contact the patient's insurance provider to verify LUMRYZ prescription benefits
- Prior to the first shipment, contact the patient to:
  - Verify he/she will receive a copy of the *Patient Brochure*
  - Counsel the patient using the *Patient Counseling Checklist* on expectations about LUMRYZ therapy and how to prepare and take LUMRYZ doses safely and effectively
  - Review important LUMRYZ safety information and precautions for LUMRYZ use
  - Review LUMRYZ safe handling and storage procedures
  - Review the adverse events associated with LUMRYZ use
  - Review the patient's use of concomitant medications
    - You will be notified of any potential for drug interactions based on patient counseling
  - Review the patient's comorbid medical conditions
  - Ask if the patient has any questions about LUMRYZ and answer the questions and/or refer the patient back to the prescriber, as appropriate
  - Provide 24/7 toll-free telephone access to pharmacist support for prescribers, office staff, and patients by answering questions about safety, dosing, and patient care
  - Dispense and ship LUMRYZ by overnight service to the patient or his/her authorized adult designee
  - Remind patients about weekly or monthly refills, as applicable
  - Contact the prescriber if a prescription refill or renewal is required

For your convenience, materials and information regarding the LUMRYZ REMS are available online at www.LUMRYZREMS.com

Please be sure to review the Prescribing Information prior to prescribing LUMRYZ for your patients.

Guidelines for Dosing and Titrating LUMRYZ

DOSING LUMRYZ

- LUMRYZ is for oral suspension in water and taken in a single dose orally at bedtime
- The recommended starting dose is 4.5 g once per night
- The recommended dosage range is 6 g to 9 g once per night
- Doses higher than 9 g per night have not been studied and should not ordinarily be administered
- The dose of LUMRYZ should be titrated to effect
  - LUMRYZ should be titrated in increments of 1.5 g per night at weekly intervals
  - The dosage may be gradually titrated based on efficacy and tolerability
- Improvement may occur during the first weeks of therapy; however, titration to an optimal dose may take longer
- Inform the patient that they should be seen by the prescriber frequently to review dose titration, symptom response, and adverse reactions; a follow-up of every three months is recommended.

NOTE: The patient's first shipment of LUMRYZ cannot exceed a 1-month (30-day) supply and future shipments cannot exceed a 3-month (90-day) supply.

DOSING AND TITRATION	
	Total Single Dose
Recommended Starting Dose	4.5 g
Effective Dosage Range	6 g
	7.5 g
	9 g

Patients who are currently being treated with immediate-release sodium oxybate may be switched to LUMRYZ at the nearest equivalent dosage in grams per night (e.g., 7.5 g sodium oxybate divided into two 3.75 g doses per night to 7.5 g LUMRYZ once per night).

Please see the LUMRYZ Prescribing Information for additional guidelines for dosing and titration.

PATIENT DOSING INFORMATION

- Inform patients that each packet of LUMRYZ contains LUMRYZ powder, which will need to be mixed with water for once-nightly dosing
- Patients should prepare the dose of LUMRYZ prior to bedtime
  - Instruct patients to make sure the LUMRYZ mixing cup is clean prior to preparing each dose
  - Each packet of LUMRYZ should be mixed with approximately 80 mL of water (to Fill Line A) in the mixing cup provided
  - After drinking the contents of the mixing cup, the patient should rinse the LUMRYZ mixing cup with an additional 25 mL of water (to Fill Line B) and drink that as well to ensure all medication is ingested
  - Patients should be instructed to store LUMRYZ in a secure place out of the reach of children and pets
- LUMRYZ should be taken at least 2 hours after eating
- LUMRYZ should be taken while in bed

Reference ID: 5166429

Additional Information About LUMRYZ

LUMRYZ has been placed in a bifurcated federal schedule. LUMRYZ is a Schedule III controlled substance when used for legitimate medical purposes, as prescribed. The active ingredient of LUMRYZ, sodium oxybate, is a gamma-hydroxybutyrate (GHB), a Schedule I controlled substance. Your patients should be informed that federal law prohibits the transfer of LUMRYZ to any persons other than the patient for whom it was prescribed. If you have any questions regarding this, please call the LUMRYZ REMS toll-free at 1-877-453-1029.

Illicit use and abuse of GHB have been reported, including in social settings (e.g., assault victims). Prescribers should carefully evaluate patients for a history of drug abuse and follow patients closely, observing them for signs of misuse or abuse of GHB (e.g., increase in size or frequency of dosing, reports of lost, stolen, or spilled medication, drug-seeking behavior, etc.).

WHEN PRESCRIBING A CONTROLLED SUBSTANCE

- Be judicious when deciding to increase a dose. Make sure the appropriate medical indicators for increasing or altering a dose are present.
- Be suspicious of a pattern of excuses for additional refills or repeated requests for additional refills on an emergency basis.
- Be vigilant. Recognize there is potential to abuse LUMRYZ. It is important you know the LUMRYZ REMS maintains records about who is prescribing LUMRYZ. These records will be made available to any state or federal agency that requests them.

DEPENDENCE AND TOLERANCE

Dependence

- Cases of severe dependence and craving for GHB have been reported when the drug is taken around the clock
- There have been case reports of withdrawal after illicit use of GHB at frequent repeated doses
    - Doses (18 g to 250 g per day) were in excess of recommended dosage range

Tolerance

- There have been some case reports of symptoms of tolerance developing after illicit use at doses far in excess of the recommended LUMRYZ dosage regimen
- Discontinuation effects and tolerance of LUMRYZ have not been systematically evaluated in controlled clinical trials

For your convenience, materials and information regarding the LUMRYZ REMS are available online at www.LUMRYZREMS.com

Reference ID: 5166429

Use in Specific Populations

PREGNANCY

There are no adequate data on the developmental risk associated with the use of sodium oxybate in pregnant women. Oral administration of sodium oxybate to pregnant rats (150, 350, or 1,000 mg/kg/day) or rabbits (300, 600, or 1,200 mg/kg/day) throughout organogenesis produced no clear evidence of developmental toxicity; however, oral administration to rats throughout pregnancy and lactation resulted in increased stillbirths and decreased offspring postnatal viability and growth, at a clinically relevant dose.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

LABOR OR DELIVERY

LUMRYZ has not been studied in labor or delivery. In obstetric anesthesia using an injectable formulation of sodium oxybate, newborns had stable cardiovascular and respiratory measures but were very sleepy, causing a slight decrease in Apgar scores. There was a fall in the rate of uterine contractions 20 minutes after injection. Placental transfer is rapid, and GHB has been detected in newborns at delivery after intravenous administration of GHB to mothers. Subsequent effects of sodium oxybate on later growth, development, and maturation in humans are unknown.

LACTATION

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.

In a study in which sodium oxybate (0, 100, 300, or 900 mg/kg/day) was orally administered to rats during the juvenile period of development (postnatal days 21 through 90), mortality was observed at the two highest doses tested. Deaths occurred during the first week of dosing and were associated with clinical signs (including decreased activity and respiratory rate) consistent with the pharmacological effects of the drug. Reduced body weight gain in males and females and delayed sexual maturation in males were observed at the highest dose tested.

GERIATRIC USE

Clinical studies of LUMRYZ or immediate-release sodium oxybate in patients with narcolepsy did not include sufficient numbers of subjects age 65 years and older to determine whether they respond differently from younger subjects. In controlled trials of immediate-release sodium oxybate in another population, 39 (5%) of 874 patients were 65 years or older. Discontinuations of treatment due to adverse reactions were increased in the elderly compared to younger adults (21% vs. 19%). Frequency of headaches was markedly increased in the elderly (39% vs. 19%). The most common adverse reactions were similar in both age categories. In general, 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

Because of an increase in exposure to LUMRYZ, LUMRYZ should not be initiated in patients with hepatic impairment because appropriate dosage adjustments for initiation of LUMRYZ 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.

MALE AND FEMALE PATIENTS

In a study of 18 female and 18 male healthy adult volunteers, no gender differences were detected in the pharmacokinetics of GHB following an immediate-release 4.5 g oral dose of sodium oxybate.

RACIAL OR ETHNIC GROUPS

There are insufficient data to evaluate any pharmacokinetic differences among races.

Please read accompanying Prescribing Information.
The LUMRYZ REMS is here to support you, your staff, and your patients.
For assistance, call 1-877-453-1029.

Patient Counseling Information

Prior to initiating therapy, counsel each patient regarding the serious risks and safe use, handling, and storage of LUMRYZ using the *Patient Brochure*.

- Inform patients that LUMRYZ is available only through certified pharmacies under a restricted distribution program called the LUMRYZ REMS and provide them with the telephone number and website for more information about LUMRYZ and the LUMRYZ REMS.
- Confirm that patients understand the serious risks and safe use conditions of LUMRYZ and that you have answered any questions the patient has about LUMRYZ by having the patient sign and date the *Patient Enrollment Form*. Inform the patient that regular follow-up is recommended.

To ensure safe and effective use of LUMRYZ, you should provide your patient with the following guidance:

ALCOHOL OR SEDATIVE HYPNOTICS

Advise patients that alcohol and other sedative hypnotics should not be taken with LUMRYZ.

SEDATION

Inform patients they are likely to fall asleep quickly after taking LUMRYZ (often within 5 minutes and usually within 15 minutes), but the time it takes to fall asleep can vary from night to night. The sudden onset of sleep, including in a standing position or while rising from bed, has led to falls resulting in injuries, in some cases requiring hospitalization. Instruct patients to remain in bed following ingestion of LUMRYZ.

FOOD EFFECT

Inform patients that LUMRYZ should be taken at least 2 hours after eating.

RESPIRATORY DEPRESSION

Inform patients that LUMRYZ can be associated with respiratory depression even at recommended doses and with concurrent use of LUMRYZ with certain other CNS depressants.

OPERATING HAZARDOUS MACHINERY

Inform patients that, until they are reasonably certain LUMRYZ does not affect them adversely (e.g., impair judgment, thinking, or motor skills), they should not engage in hazardous occupations or activities requiring complete mental alertness or motor coordination, such as operating hazardous machinery or a motor vehicle or flying an airplane, for at least 6 hours after taking LUMRYZ.

SUICIDALITY

Instruct patients to contact a healthcare provider immediately if the patient develops depressed mood, markedly diminished interest or pleasure in usual activities, significant change in weight and/or appetite, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, or suicidal ideation.

SLEEPWALKING

Instruct patients that LUMRYZ has been associated with sleepwalking and other behaviors during sleep, and to contact their healthcare provider if this occurs.

SODIUM INTAKE

Instruct patients that LUMRYZ contains a significant amount of sodium and patients who are sensitive to sodium intake (e.g., those with heart failure, hypertension, or renal impairment) should limit their sodium intake.

SAFE USE, HANDLING, STORAGE, AND DISPOSAL

- Discuss safe and proper use of LUMRYZ and dosing information with patients prior to the initiation of treatment.
- Instruct patients to store LUMRYZ packets in a secure place, out of reach of children and pets.
- Instruct patients to take one dose nightly at bedtime. Patients should not divide dose.
- Inform patients they should be seen by their healthcare provider frequently to review dose titration, symptom response, and adverse reactions.
- Instruct patients to store LUMRYZ at room temperature, between 59°F and 86°F. Inform patients they may safely dispose of LUMRYZ down the sink.
- Inform patients they must report all instances of lost or stolen LUMRYZ to the local police and to the LUMRYZ REMS.

Reference ID: 5166429

Lumryz™

(sodium oxybate) for extended-release oral suspension CIII

Avadel™

Phone: 1-877-453-1029 | www.LUMRYZREMS.com | Fax: 1-877-206-3198

MED-US-LUM-2100004
[REMS Approval Date]

LUMRYZ™ REMS

PATIENT BROCHURE

Important information about the safe use and handling of LUMRYZ (sodium oxybate) for extended-release oral suspension

Lumryz™

(sodium oxybate) for extended-release oral suspension

Learn more scan to enroll.

Reference ID: 5166429

Lumryz.

(sodium oxybate) for extended-release oral suspension C

Dear Patient,

You are receiving these materials because your healthcare provider has prescribed LUMRYZ (sodium oxybate) for extended-release oral suspension for you. LUMRYZ is a medicine used to treat excessive daytime sleepiness and/or cataplexy in adults with narcolepsy.

The Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for LUMRYZ because of the serious risks associated with LUMRYZ. The purpose of the LUMRYZ REMS is to make sure the benefits of LUMRYZ outweigh the risks. All patients must be enrolled in the LUMRYZ REMS to receive LUMRYZ. This *Patient Brochure* contains information you need to know about LUMRYZ and will help you to use LUMRYZ correctly. Read this *Patient Brochure* before you start taking LUMRYZ.

After your healthcare provider sends your enrollment form to the LUMRYZ REMS and your first prescription for LUMRYZ to your certified pharmacy, you will receive a call from your certified pharmacy to tell you how to get started with taking LUMRYZ and to answer any questions you may have about LUMRYZ.

You will also speak with appropriate staff at a certified pharmacy, who will go over your insurance information with you. Before you can receive your first shipment of LUMRYZ, a pharmacist at a certified pharmacy must confirm whether you have read and understood this *Patient Brochure*, ask you about your medical history and other medications you may be taking, and give you advice on how to prepare and take your LUMRYZ and how to store it safely. **You must take this call before you can get your LUMRYZ.**

Please call your healthcare provider if you have questions about LUMRYZ, or you can contact the LUMRYZ REMS toll free at 1-877-453-1029. You can reach your certified pharmacy 24 hours a day, 7 days a week with any questions. We hope you find this information and the LUMRYZ REMS services helpful.

Sincerely,

Avadel CNS Pharmaceuticals, LLC

WARNING: LUMRYZ can cause serious side effects.
Do not drink alcohol or take other medicines that make you sleepy.

LUMRYZ is a prescription medicine used to treat adults with narcolepsy to reduce excessive daytime sleepiness and/or cataplexy (suddenly weak or paralyzed muscles).

IMPORTANT INFORMATION ABOUT LUMRYZ INCLUDES THE FOLLOWING:

- When taking LUMRYZ, **do not** drink alcohol or take other medicines that slow your breathing or mental activity or make you sleepy. You could have serious side effects.
- LUMRYZ can cause serious side effects, including trouble breathing while asleep, confusion, unusual or disturbing thoughts, depression, and passing out, even at recommended doses. Tell your healthcare provider if you have any of these problems while taking LUMRYZ.
- Abuse of LUMRYZ can lead to dependence (a physical need to take the drug), craving for the medicine, and severe withdrawal symptoms (symptoms that start when the drug is stopped, especially when it is stopped suddenly).
- Each packet of LUMRYZ contains LUMRYZ powder, which will need to be mixed with water for once-nightly dosing prior to bedtime.
- Take 1 packet of LUMRYZ each day at bedtime.
- Mix and take LUMRYZ within 30 minutes. If not taken within 30 minutes of mixing, throw it away (dispose of it) and prepare a new dose.
- Avoid getting out of your bed after taking LUMRYZ. Some people fall asleep within 5 minutes of taking LUMRYZ and most will fall asleep within 15 minutes. The time it takes you to fall asleep might be different from night to night.
- **Do not** drive a car, use heavy machinery, fly an airplane, or do anything dangerous or that requires you to be alert for at least 6 hours after taking LUMRYZ. When you first start taking LUMRYZ, be careful until you know how LUMRYZ affects you.
- Keep LUMRYZ out of the reach of children and pets. Get emergency medical help right away if a child ingests LUMRYZ.
- Report all side effects to your healthcare provider.

WHAT WILL YOU FIND IN THIS BROCHURE?

This brochure answers important questions about how to get your LUMRYZ, how to use LUMRYZ properly, and how to store it safely. It also gives you important information about LUMRYZ.

WHAT IS THE LUMRYZ REMS?

The FDA has required a special program called a REMS for LUMRYZ because of the serious risks associated with LUMRYZ. Enrollment in the LUMRYZ REMS by prescribers, pharmacies, and patients is required by the FDA to ensure the benefits of LUMRYZ outweigh the risks associated with LUMRYZ. You are enrolled in the REMS when your healthcare provider sends the *Patient Enrollment Form* you signed to the LUMRYZ REMS. Your healthcare provider can then send your prescription for LUMRYZ to a certified pharmacy.

Certified pharmacy staff will review important information about LUMRYZ with you. They will also answer any questions you have about LUMRYZ.

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ENROLLING IN THE LUMRYZ REMS

WHAT AM I REQUIRED TO DO IN THIS REMS?

As a patient, your responsibility is to discuss the safe use of LUMRYZ with your healthcare provider and to read this *Patient Brochure* before receiving your first LUMRYZ prescription. Be sure to let your healthcare provider know if you are taking other medications or if you have any conditions that might affect your breathing.

DO I HAVE TO ENROLL IN THIS REMS?

You and your healthcare provider will be required to sign a *Patient Enrollment Form* in order to receive LUMRYZ. You must verify that you have been counseled by your healthcare provider on the serious risks and safe use of LUMRYZ and that you were able to ask your healthcare provider any questions you have about LUMRYZ.

FILLING YOUR LUMRYZ PRESCRIPTION

HOW IS MY PRESCRIPTION FILLED?

All LUMRYZ prescriptions are filled only by pharmacies certified in the LUMRYZ REMS.

WHAT DOES A CERTIFIED PHARMACY DO?

Your healthcare provider sends your LUMRYZ prescription directly to a certified pharmacy.

After your healthcare provider sends in your first prescription of LUMRYZ, you will receive a call from your certified pharmacy to tell you how to get started with taking LUMRYZ and to answer any questions you may have about LUMRYZ. A staff member from your certified pharmacy will call you to complete a *Patient Counseling Checklist*. The *Patient Counseling Checklist* will include information about other medications you are taking and other medical conditions that might increase your risk of serious side effects. Your certified pharmacy will go over the information about how to use LUMRYZ safely and provide a copy of this brochure with your first shipment.

Your certified pharmacy will always ask you where and when you would like your LUMRYZ delivered and who will sign for the shipment. LUMRYZ will be shipped by an overnight service. When the courier arrives, you or an adult you designate must sign for your LUMRYZ.

WHAT WILL I GET WITH MY LUMRYZ PRESCRIPTION?

With each prescription, you will get a carton containing individual, dose packets of LUMRYZ (each child-resistant dose packet contains one single dose of LUMRYZ, all of the same dose strength), a LUMRYZ-specific mixing cup for mixing your LUMRYZ dose with water in preparation for drinking the mixture, and a cap to close the mixing cup and assist with mixing (e.g., shaking or otherwise agitating the LUMRYZ and water after being placed in the mixing cup).

HOW DO I GET MY LUMRYZ REFILLS?

Your certified pharmacy will contact you when it is close to your refill time. You may also call your certified pharmacy to schedule your refills.

CAN MY LOCAL PHARMACY PROVIDE LUMRYZ?

No. You can get your LUMRYZ only from a LUMRYZ REMS certified pharmacy. You may be able to have your LUMRYZ shipped to your home, place of work or to a local overnight carrier hub for pickup. Saturday deliveries may also be an option for you. Your certified pharmacy will work with you on the options available.

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INSURANCE COVERAGE

WILL INSURANCE PAY FOR MY LUMRYZ?

In most cases, yes. A staff member from your certified pharmacy will call and work with your insurance company to help you get coverage for LUMRYZ. In the unlikely event your insurance does not cover LUMRYZ or you can't afford the out-of-pocket costs, ask the certified pharmacy about available financial assistance programs.

WHAT IS THE PHARMACY'S ROLE WITH MY INSURANCE?

An experienced pharmacy staff member will:

- Contact you to go over your prescription benefits and coverage
- Tell you what your co-pay is, if applicable
- Tell you about any LUMRYZ prescription savings plans for which you may qualify
- Work with your healthcare provider on prior authorizations, if required by your insurance company
- Provide information about any financial help that may be available to you

Your certified pharmacy's attempt to get coverage from a third-party payer does not guarantee that you will get coverage.

WHAT SHOULD I DO WHEN I GET MY LUMRYZ CARTON?

Before using a new LUMRYZ carton, check the tamper-evident seal on the carton lid to make sure it is not missing or broken. **Do not** use if the tamper-evident seal is missing or broken.

Check the expiration date (EXP) on the side of the LUMRYZ carton. **Do not** use LUMRYZ after the expiration date (EXP) on the label has passed.

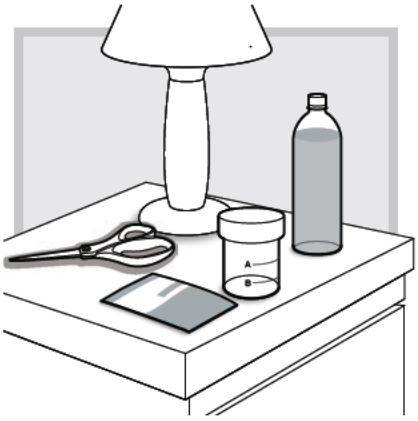
Open the LUMRYZ carton by tearing the tamper-evident seal with your hands or by using a pair of scissors.

BEFORE EACH USE

- Clean the mixing cup by rinsing it with water and letting it dry before each use.
- **Do not** use a measuring device other than the mixing cup that comes in your LUMRYZ carton to measure and take a dose of LUMRYZ.
- Check the expiration date (EXP) on the packet label. **Do not** use the LUMRYZ packet after the expiration date (EXP) has passed.

Important: **Make sure to prepare LUMRYZ at bedside.**

Gather the following supplies and place them on a flat surface at your bedside:



- 1 bottle or glass of water (1/3 cup). Do not use hot water.
- 1 LUMRYZ packet
- 1 clean mixing cup. - The cap is not child resistant.
- 1 pair of scissors (optional)

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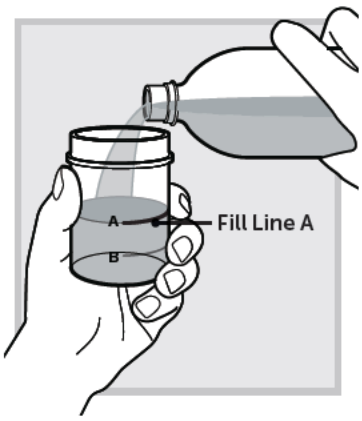
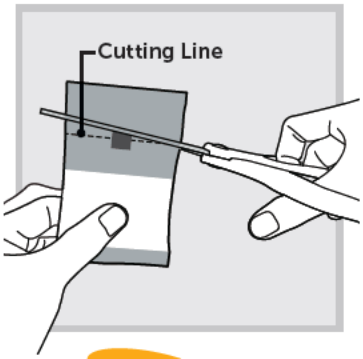
HOW DO I TAKE MY LUMRYZ?

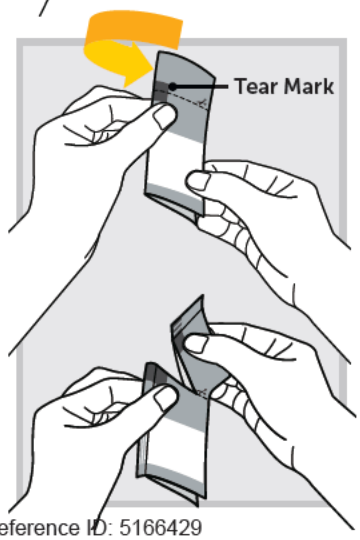
MIX THE LUMRYZ SOLUTION AT YOUR BEDSIDE

1 At your bedside, open the mixing cup by twisting the cap to the left (counter-clockwise) to remove it.



2 Fill the mixing cup with water up to **Fill Line A** (top line) and set the mixing cup down on a flat surface.



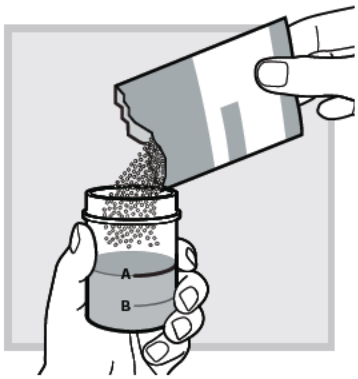


3 Open 1 packet:

- Use scissors to cut open the packet along the **Cutting Line**, located on the back of the packet.

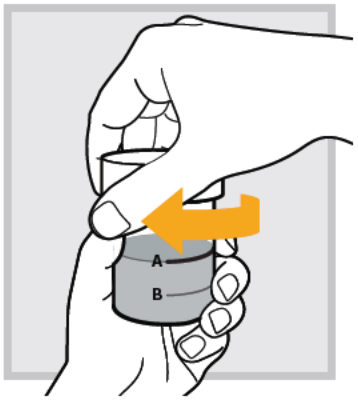
-or-

- Fold the packet in half at the gray **Tear Mark** located on the back of the packet.
- Tear the packet open with your hands.

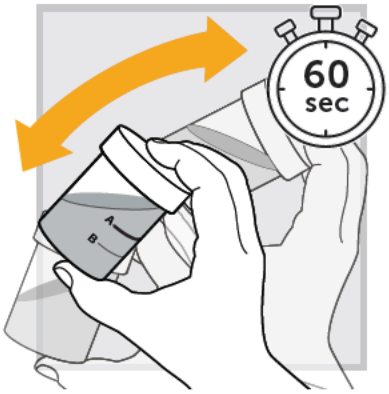


4 Pour the entire content from the packet into the water-filled mixing cup.

Make sure there is no powder left in the packet.



5 Close the mixing cup by twisting the cap to the right (clockwise) until firmly closed.



6 Mix the water and powder solution by shaking the closed mixing cup well for at least **60 seconds (1 minute)**.

7 Make sure the solution is mixed thoroughly.

The mixed solution will appear slightly milky with some lumps.

The mixing cup cap is not child resistant. If the mixed solution is not drank immediately, then do not remove the cap, and keep out of reach of children.

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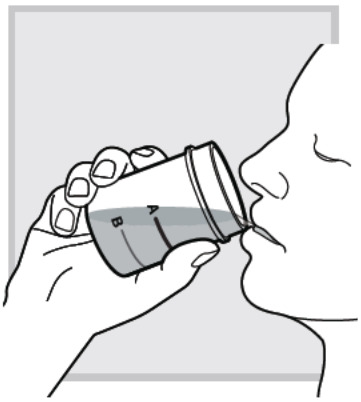
HOW DO I TAKE MY LUMRYZ?

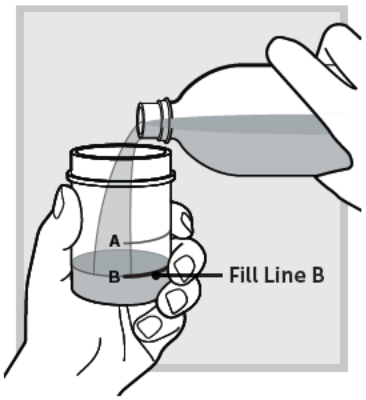
TAKE THE LUMRYZ SOLUTION AT YOUR BEDSIDE

8 Open the mixing cup by twisting the cap to the left (counter-clockwise) and remove it.



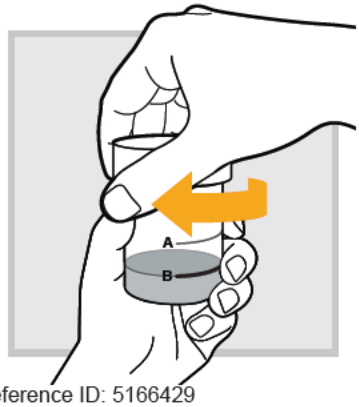
9 While sitting in bed drink the mixed solution within **30 minutes** of mixing.

Make sure to drink all the mixed solution in the mixing cup.

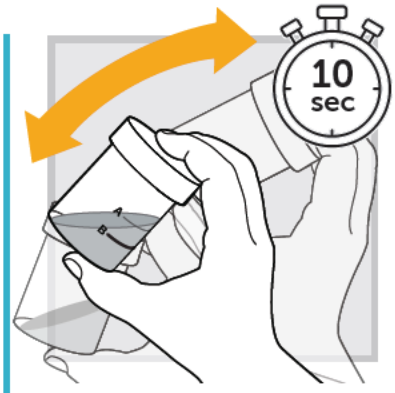


10 Immediately refill your mixing cup with water up to **Fill Line B** (lower line) to mix in any medicine left in the mixing cup.

Do not open another packet of LUMRYZ. Take only 1 packet each day at bedtime.



11 Close the mixing cup by twisting the cap to the right (clockwise) until firmly closed.

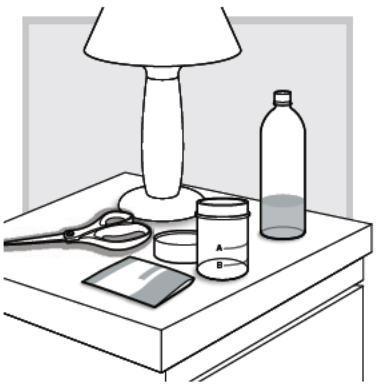


12 Shake well again for **10 seconds.**

13 Open the mixing cup by twisting the cap to the left (counter-clockwise) and remove it.

14 Drink the mixed solution immediately after mixing.

Make sure to drink all the mixed solution in the mixing cup.



15 Leave the empty mixing cup at your bedside and immediately lie down to go to sleep.

Avoid getting out of your bed after taking your dose.

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WHAT SHOULD I DO IF I MISS A DOSE?

It is very important to take only one single dose of LUMRYZ each day at bedtime, as prescribed. If you miss a dose, skip that dose.

- Do not take LUMRYZ again until the next day at bedtime.

Empty any unused LUMRYZ solution that you prepared but did not take down the sink the next day. Clean the mixing cup by rinsing it with water and letting it dry before each use.

HOW SOON WILL I SEE A CHANGE IN MY SYMPTOMS?

After starting LUMRYZ, it may take a few weeks or longer to see your symptoms improve. It may also take time to find the right dose that works for you. It is important that you talk with your healthcare provider often when you first start taking LUMRYZ.

Tell your healthcare provider if you don't feel any improvements while taking LUMRYZ. LUMRYZ may not be right for you.

WHAT ARE THE SIDE EFFECTS OF LUMRYZ?

LUMRYZ can cause serious side effects, including breathing problems (slower breathing, trouble breathing, and short periods of no breathing while asleep), mental health problems (confusion, seeing or hearing things that are not real, unusual or disturbing thoughts, feeling anxious or upset, depression, thoughts of suicide, increased tiredness, feelings of guilt or worthlessness, difficulty concentrating), and sleepwalking. If you have any of these side effects, call your healthcare provider right away.

The most common side effects with LUMRYZ are nausea, dizziness, bedwetting, headache, and throwing up.

These are not the only possible side effects with LUMRYZ. If you are worried about any possible side effects with LUMRYZ, talk with your healthcare provider or a pharmacist at a certified pharmacy.

ARE THERE ANY PRECAUTIONS I SHOULD TAKE WHILE ON LUMRYZ?

- While taking LUMRYZ, do not drink alcohol or take medicines that cause sleepiness.
- Do not drive a car, use heavy machinery, or do anything that is dangerous or requires you to be alert, for the first 6 hours after taking LUMRYZ.
- When you first start taking LUMRYZ, be careful until you know how it will affect you.
- Before starting LUMRYZ, tell your healthcare provider if you are pregnant, or plan to become pregnant, or if you are breastfeeding. It is not known whether LUMRYZ can pass through your breast milk.
- Keep LUMRYZ in a safe place, out of the reach of children.
- Take LUMRYZ while in bed.

Tell your healthcare provider and pharmacist about any other medicines you are taking, including prescription and non-prescription medicines, vitamins, and supplements.

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It is also important to tell other healthcare providers, including pharmacists, that you are taking LUMRYZ before you start or change any medications.

HOW OFTEN SHOULD MY HEALTHCARE PROVIDER CHECK MY PROGRESS WITH LUMRYZ?

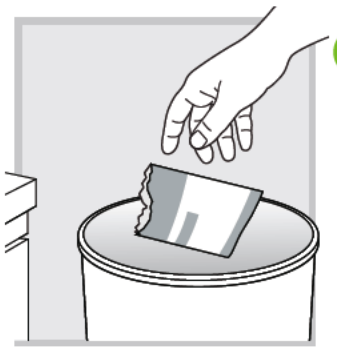
When you first start taking LUMRYZ, you may need to talk to your healthcare provider often until he/she determines the best dose for you. It is possible your dose may need to be adjusted. Your healthcare provider will evaluate you within the first 3 months of taking LUMRYZ and may reevaluate you every 3 months while you are taking LUMRYZ.

STORAGE AND SAFETY TIPS AT HOME

HOW DO I STORE LUMRYZ?

- Always store LUMRYZ in its original carton in a clean dry place.
- Store LUMRYZ at room temperature, between 68°F to 77°F (20°C to 25°C), and do not refrigerate or allow near fire.
- Keep LUMRYZ and all medicines out of reach of children and pets. If a child or pet ingests LUMRYZ, get emergency medical help (call 911) right away.

HOW DO I THROW AWAY (DISPOSE OF) LUMRYZ?



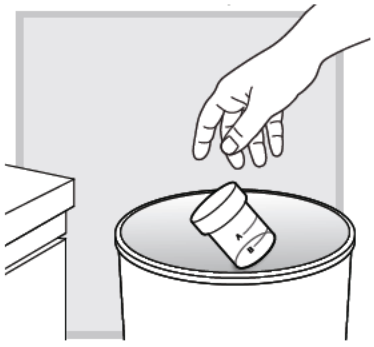
1 The next day, place the empty LUMRYZ packet in the trash.

If any LUMRYZ remains in the packet, rinse it down the sink prior to disposal.

2 Empty any unused LUMRYZ down the sink drain the next day.

Clean the mixing cup by rinsing it with water and letting it dry before each use.

After you finish all of the packets in your LUMRYZ carton



After you have finished your last packet in the carton, throw away the rinsed mixing cup in the trash.

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WHAT IF I HAVE CONCERNS ABOUT HAVING LUMRYZ IN MY HOME?

- If your LUMRYZ is lost or stolen, report the incident right away to the local police and to your certified pharmacy.
- Use LUMRYZ only as your healthcare provider tells you. Remember that use of your LUMRYZ by others is illegal.
- If you have any questions or concerns, or if you need advice about LUMRYZ, call your healthcare provider or your certified pharmacy.

GETTING MORE INFORMATION

WHERE CAN I GET MORE INFORMATION ABOUT LUMRYZ?

For more information about LUMRYZ, contact the LUMRYZ REMS:

Phone: 1-877-453-1029

Fax: 1-877-206-3198

Website: www.LUMRYZREMS.com

Reference ID: 5166429

NOTES

KEEP THIS BOOKLET AS A HELPFUL REMINDER

If you have questions or need information, contact the LUMRYZ REMS at 1-877-453-1029.

Lumryz™

(sodium oxybate) for extended-release oral suspension CIII

Avadel™

Phone: 1-877-453-1029 | www.LUMRYZREMS.com | Fax: 1-877-206-3198

MED-US-LUM-2100005
[REMS Approval Date]

LUMRYZ™ REMS

Certified Pharmacy Training — Pharmacy Staff and Pharmacists

All LUMRYZ REMS certified pharmacy staff and pharmacists involved in dispensing LUMRYZ must complete the **Pharmacy Staff Module** and the *Pharmacy Staff Knowledge Assessment*. Pharmacists must also complete the **Pharmacist Module** and the *Pharmacist Knowledge Assessment*.

Lumryz™

(sodium oxybate) for extended-release oral suspension Ⓒ

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Lumryz™

(sodium oxybate) for extended-release oral suspension [C]

Dear LUMRYZ REMS Certified Pharmacy Staff,

The LUMRYZ REMS has been approved by the Food and Drug Administration (FDA) as a Risk Evaluation and Mitigation Strategy (REMS).

The LUMRYZ REMS

The FDA has determined that a REMS is necessary to ensure that the benefits of LUMRYZ (sodium oxybate) for extended-release oral suspension outweigh the risks of serious adverse outcomes resulting from inappropriate prescribing, misuse, abuse, and diversion of LUMRYZ by:

1. **Informing prescribers, pharmacists, and patients of:**
   - The risk of significant central nervous system (CNS) and respiratory depression associated with LUMRYZ
   - The contraindication of use of LUMRYZ with sedative hypnotics or alcohol
   - The potential for abuse, misuse, and overdose associated with LUMRYZ
   - The safe use, handling, and storage of LUMRYZ
2. **Ensuring that pharmacy controls exist prior to filling prescriptions for LUMRYZ that:**
   - Screen for concomitant use of sedative hypnotics and other CNS depressants
   - Monitor for inappropriate prescribing, misuse, abuse, and diversion of LUMRYZ
   - Notify prescribers when patients are receiving concomitant contraindicated medications or when there are signs of potential abuse, misuse, or diversion

This training provides information about the LUMRYZ REMS that includes important information about LUMRYZ and the responsibilities of certified pharmacy staff involved in the dispensing of LUMRYZ.

LUMRYZ is approved for:

- Treatment of cataplexy in adults with narcolepsy
- Treatment of excessive daytime sleepiness (EDS) in adults with narcolepsy

LUMRYZ may be prescribed only by prescribers certified in the LUMRYZ REMS and dispensed only by pharmacies certified in the LUMRYZ REMS to patients enrolled in the LUMRYZ REMS. Please contact the LUMRYZ REMS with any questions at www.LUMRYZREMS.com or 1-877-453-1029.

Sincerely,

Avadel CNS Pharmaceuticals, LLC

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CERTIFIED PHARMACY TRAINING — PHARMACY STAFF MODULE

LUMRYZ™ REMS

Training for Pharmacy Staff Involved in the LUMRYZ REMS

All pharmacy staff within a LUMRYZ REMS certified pharmacy involved in dispensing LUMRYZ must complete training on the **Pharmacy Staff Module** successfully complete the *Pharmacy Staff Knowledge Assessment*. Training must be completed annually.

Lumryz™

(sodium oxybate) for extended-release oral suspension Ⓒ

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IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE

- LUMRYZ (sodium oxybate) for extended-release oral suspension is a central nervous system (CNS) depressant that is indicated for the following:
  - Treatment of cataplexy in adults with narcolepsy
  - Treatment of excessive daytime sleepiness (EDS) in adults with narcolepsy

HOW SUPPLIED

- LUMRYZ is shipped from a LUMRYZ REMS certified pharmacy directly to patients. Each shipment to a patient will contain:
  - A carton with the prescribed amount of LUMRYZ packets at the prescribed dose (each child-resistant package contains a packet of LUMRYZ 4.5 g, 6 g, 7.5 g, or 9 g)
  - A mixing cup for preparation of each single dose (LUMRYZ dose mixed with water)
  - For a new patient, the *Patient Brochure*

CONTROLLED SUBSTANCE SCHEDULING

- The active ingredient in LUMRYZ is sodium oxybate or gamma-hydroxybutyrate (GHB, a known drug of abuse). GHB has been used to facilitate sexual assaults. Because of its rapid sedative effects (particularly when mixed with alcohol) and its colorless and odorless appearance, GHB has been used to "spike" the drinks of unsuspecting victims. Because of its abuse potential, GHB is designated a controlled substance by the Drug Enforcement Administration (DEA) and has been placed in a bifurcated federal schedule.
- GHB products approved by the FDA, such as sodium oxybate, and used as prescribed for therapeutic purposes are Schedule Ill drugs.
- The active ingredient of LUMRYZ, sodium oxybate, is the sodium salt of GHB, a Schedule I controlled substance.
- Federal law prohibits the transfer of LUMRYZ to any persons other than the patient for whom it was prescribed.

BOXED WARNING

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 sodium oxybate during clinical trials in narcolepsy were receiving central nervous system 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, decreases in the level of 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. For further information go to www.LUMRYZREMS.com or call 1-877-453-1029.

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IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- LUMRYZ is contraindicated for use in:
  - combination with sedative hypnotics.
  - combination with alcohol.
  - patients with succinic semialdehyde dehydrogenase deficiency, a rare disorder of inborn error of metabolism variably characterized by mental retardation, hypotonia, and ataxia.

WARNINGS AND PRECAUTIONS

Central Nervous System Depression

- LUMRYZ is a CNS depressant.
- 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.
  - If short-term use of an opioid (e.g., post- or perioperative) is required, interruption of treatment with LUMRYZ should be considered.
- Patients who have sleep apnea or compromised respiratory function may be at a higher risk of developing respiratory depression, loss of consciousness, coma, and death with LUMRYZ use.
- Healthcare providers should caution patients about operating hazardous machinery, including automobiles or airplanes, until they are reasonably certain that LUMRYZ does not affect them adversely (e.g., impair judgment, thinking, or motor skills). Patients should not engage in hazardous occupations or activities requiring complete mental alertness or motor coordination, such as operating machinery or a motor vehicle or flying an airplane, for at least 6 hours after taking LUMRYZ.

Abuse, Misuse and Diversion

- LUMRYZ is a Schedule III controlled substance.
- The active ingredient of LUMRYZ, sodium oxybate, is the sodium salt of 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 (e.g., assault victim).
- Patients should be carefully evaluated for a history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of GHB (e.g., increase in size or frequency of dosing, reports of lost, stolen, or spilled medication, drug-seeking behavior, feigned cataplexy).

For complete safety information, please see the Prescribing Information for LUMRYZ.

Reference ID: 5166429

LUMRYZ REMS REQUIREMENTS

LUMRYZ may be prescribed only by prescribers certified in the LUMRYZ REMS and dispensed only to patients enrolled in the LUMRYZ REMS. Because of the risks of CNS depression, abuse, misuse, and diversion, LUMRYZ is available only through a restricted program called the LUMRYZ REMS.

Notable requirements of this REMS include:

- Use of a certified pharmacy.
- Healthcare providers who prescribe LUMRYZ must have completed the *Prescriber Enrollment Form* and must comply with the requirements of the LUMRYZ REMS.
- To receive LUMRYZ, patients must be enrolled in the LUMRYZ REMS and be counseled on the serious risks and safe use of LUMRYZ treatment. Patients are enrolled by certified prescribers who must fill out and submit the *Patient Enrollment Form*. Prescribers must also complete and submit the *Prescription Form* to a certified pharmacy for all new LUMRYZ prescriptions and for LUMRYZ prescriptions for patients restarting LUMRYZ treatment after not receiving LUMRYZ for 6 months or more.

Further information is available at www.LUMRYZREMS.com.

OVERVIEW OF CERTIFIED PHARMACY RESPONSIBILITIES

ENROLLMENT VERIFICATION

- The *Prescriber Enrollment Form* and the *Patient Enrollment Form* are sent to the LUMRYZ REMS by the prescriber.
- Information from the enrollment forms is maintained in the appropriate LUMRYZ REMS database by the LUMRYZ REMS.
- No duplicate patients may be enrolled.
- The LUMRYZ REMS will notify the prescriber of successful certification in the LUMRYZ REMS, and that he/she is eligible to prescribe LUMRYZ.
  - If there is a delay in shipping while a question about the prescriber's credentials is being resolved, the patient will be notified by his/her certified pharmacy.
  - If the prescription cannot be filled because a question about the prescriber's credentials could not be resolved, the patient will be notified by his/her certified pharmacy.
  - The prescriber will be notified by the LUMRYZ REMS that he/she cannot be certified due to credential verification failure.
- Patients must confirm they have been counseled on the serious risks and safe use of LUMRYZ; the certified pharmacy will also provide counseling for new patients, existing patients who restart treatment after not receiving LUMRYZ for 6 months or longer, and patients who report a change in their medication or medical history.
- Enrollment status is maintained in the LUMRYZ REMS.
  - The LUMRYZ REMS will confirm that the prescriber's DEA, State License, and NPI numbers are active and that the prescriber has provided all REMS-required attestations.
  - A prescriber may be disenrolled from the REMS for expired DEA or NPI or for noncompliance with the LUMRYZ REMS.
  - Following enrollment, the patient remains in the LUMRYZ REMS unless his/her certified pharmacy and/or certified prescriber determine that the patient should be disenrolled.
- A certified prescriber and/or a certified pharmacy can request that a patient be disenrolled from the LUMRYZ REMS.
  - A patient may be disenrolled from the REMS for noncompliance with the LUMRYZ REMS, including multiple suspicious early refill requests, or other information indicating abuse, misuse, or diversion.
  - The LUMRYZ REMS will contact a prescriber if an enrollment form is received for a patient previously disenrolled from the REMS, or for suspicions of abuse, misuse, or diversion, and will provide the prescriber with all relevant patient history.

PRESCRIPTION PROCESSING

- A certified pharmacy must validate all prescriptions prior to dispensing LUMRYZ. Before a prescription for LUMRYZ can be shipped to a patient, the certified pharmacy must:
  - Verify that the *Prescription Form* is complete and signed by the prescriber.
  - Verify that the *Prescription Form* was received from the prescriber's office.
  - Verify the prescription is dated according to state-controlled substance regulations.
  - Verify the prescription is for no more than a 1-month (30-day) supply on a patient's first LUMRYZ fill and no more than a 3-month (90-day) supply on subsequent fills.
  - Verify there are no discrepancies or concerns with the dosing and titration.
    - If there are discrepancies or concerns, the certified pharmacy must contact the prescriber to revise and resubmit the prescription.
  - Review the patient information contained in the LUMRYZ REMS patient database using the secure web viewing portal and the *Prescription Form*, including:
    - Comorbid conditions and concomitant use of sedative hypnotics, certain other CNS depressants or other potentially interacting agents that either are unknown to the prescriber or pose a high risk of serious interaction with LUMRYZ.
      - If comorbid conditions or patient use of a contraindicated medication is confirmed and if the prescriber has not indicated prior knowledge, then the pharmacist will notify and consult the prescriber about the comorbid conditions and risks of concomitant medication use and document the call and the prescriber's treatment rationale on the *Patient Counseling Checklist*.
    - Alerts and *Risk Management Reports (RMRs)* regarding potential abuse, misuse, or diversion.
  - Contact the other REMS for oxybate products by phone to:
    - Verify that the patient has no other active, overlapping prescriptions for oxybate products that overlap with the current prescription.
    - Verify that the patient and prescriber have not been disenrolled from any other REMS for oxybate products for suspected abuse, misuse, or diversion.
  - Document that the calls to the other REMS for oxybate products were completed by submitting confirmation to the LUMRYZ REMS through the pre-dispense authorization (PDA) process.
  - Obtain a PDA from the LUMRYZ REMS upon receipt of a *Prescription Form*. The issuance of a PDA informs the pharmacy that the prescriber is certified, the patient is enrolled in the LUMRYZ REMS, and the patient has no other active, overlapping LUMRYZ prescriptions. The PDA also indicates that the pharmacy confirmed that the call was made to the other REMS for oxybate products to verify the patient has no other active, overlapping prescriptions for oxybate products that overlap with the current prescription for LUMRYZ and that the patient and prescriber has not been disenrolled from any other REMS for oxybate products for suspected abuse, misuse, or diversion, as described above. The PDA also indicates that the pharmacy confirmed that each prescription filled for LUMRYZ is reported to each REMS for oxybate products.
    - The certified pharmacy will process all LUMRYZ prescriptions, regardless of payment method, through the pharmacy management system (PMS) and obtain a PDA via electronic verification to verify the prescriber is certified, the patient is enrolled in the LUMRYZ REMS, the patient has no other active, overlapping LUMRYZ prescriptions, and the pharmacy confirmed that a call was made to the other REMS for oxybate products to

verify the patient has no other active, overlapping prescriptions for oxybate products that overlap with the current prescription for LUMRYZ and that the patient and prescriber has not been disenrolled from any other REMS for oxybate products for suspected abuse, misuse, or diversion, and the pharmacy confirmed that each prescription filled for LUMRYZ is reported to each REMS for oxybate products as described above.

- To verify the safe use conditions electronically through the PMS, the following prescription information, at a minimum, is required to be submitted upon processing every LUMRYZ prescription. A PDA can also be obtained by accessing the secure pharmacy portal on the LUMRYZ REMS website or by calling the LUMRYZ REMS.
  - Patient First Name
  - Patient Last Name
  - Patient Date of Birth
  - Patient Zip Code
  - Prescriber Identifier on prescription (NPI or DEA)
  - Date of Fill
  - Days' Supply
  - Quantity
  - Product/NDC
  - Confirmation that a call was made to the other REMS for oxybate products
  - Confirmation that each prescription filled for LUMRYZ is reported to each REMS for oxybate products.
- If all safe use conditions are met, a PDA will be generated by the LUMRYZ REMS. The PDA will be maintained in the LUMRYZ REMS patient database. The certified pharmacy is authorized to dispense LUMRYZ upon receiving a PDA provided all other dispensing requirements are met.
- If the safe use conditions are not met, a PDA will not be issued, and the pharmacy will be notified of the reason why:
  - Pharmacy is not certified
  - Prescriber is not certified
  - Patient is not enrolled
  - Patient has an active, overlapping prescription for LUMRYZ
  - Pharmacy did not confirm that a call was made to the other REMS for oxybate products to verify the patient has no other active, overlapping prescriptions for oxybate products that overlaps with the current prescription for LUMRYZ, and that the patient and prescriber has not been disenrolled from any other REMS for oxybate products for suspected abuse, misuse, or diversion
  - Pharmacy did not confirm that each prescription filled for LUMRYZ was reported to each REMS for oxybate products.

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- If a certified pharmacy receives information regarding overlapping prescriptions for an oxybate product for a patient, the certified pharmacy responsible for dispensing the current prescription will notify and consult each prescriber.
  - Prescriptions are considered overlapping when more than one prescription for an oxybate product is dispensed for a patient within an overlapping timeframe.
    - If a certified pharmacy suspects abuse, misuse, or diversion, the prescription should not be filled, the certified pharmacy must complete and submit a *RMR* to the LUMRYZ REMS, and the prescriber will be notified.
    - There are valid reasons why a patient may have overlapping prescriptions on file or on hold, including if the patient moves or changes prescribers, or if the prescriber sends in a new prescription prior to the completion of all refills.
    - A certified pharmacy responsible for dispensing LUMRYZ to a patient must ensure that under these situations a patient does not receive multiple overlapping shipments of an oxybate product.
    - There are valid reasons why a patient may need an overlapping dispense of an oxybate product, including if the prescriber is changing the patient's treatment, to avoid delivery issues, if there is a valid early refill (e.g., lost or stolen medication), or for titration timing.
- Once a PDA is obtained from the LUMRYZ REMS, review of the patient information in the patient database using the secure web viewing portal has been performed, and the other REMS for oxybate products have been contacted, the certified pharmacy will contact the patient to schedule shipment and complete the required counseling.
  - For a new patient, the certified pharmacy provides the *Patient Brochure*.
  - A pharmacist must counsel the patient by completing the *Patient Counseling Checklist* prior to the initial dispensing of LUMRYZ.
    - The certified pharmacy must submit the *Patient Counseling Checklist* to the LUMRYZ REMS online at www.LUMRYZREMS.com or complete a print version and fax to the LUMRYZ REMS at 1-877-206-3198.
- A certified pharmacy must not stock LUMRYZ in retail pharmacies.

SHIPPING

All LUMRYZ is shipped to patients (or their adult designee) by an overnight service with receipt signature required. Certified pharmacies must provide confirmation of receipt of each prescription of LUMRYZ to the LUMRYZ REMS by accessing the LUMRYZ REMS website (www.LUMRYZREMS.com) or calling the LUMRYZ REMS at 1-877-453-1029.

- The patient may request an alternate shipping address, which is subject to approval by a pharmacist.
- See **How Supplied** for details of the contents of each LUMRYZ shipment.
- Daily tracking reports are generated to confirm the receipt of each order shipped.
- Lost shipments are investigated.

MONITORING FOR INAPPROPRIATE PRESCRIBING, ABUSE, MISUSE, AND DIVERSION

Certified pharmacies must conduct detailed monitoring on an ongoing basis of patients and prescribers for signs of inappropriate prescribing, abuse, misuse and diversion. Each certified pharmacy will:

- Document early refill requests and instances of patient and prescriber behavior that suggest potential abuse, misuse, or diversion by completing and submitting a *RMR* to the LUMRYZ REMS online at www.LUMRYZREMS.com or complete a print version and fax to the LUMRYZ REMS at 1-877-206-3198. This information is maintained in the prescriber and/or patient databases in the LUMRYZ REMS.
  - Request the LUMRYZ REMS to disenroll a patient who has demonstrated behavior that suggests potential abuse, misuse, or diversion by completing and submitting a *RMR* to the LUMRYZ REMS.
  - Recommend that a prescriber who has demonstrated behavior that suggests potential abuse, misuse, or diversion be disenrolled by submitting a *RMR* to the LUMRYZ REMS.
- Review the patient's *RMR* history and alerts in the LUMRYZ REMS using the secure pharmacy web viewing portal for the patient database prior to granting an early refill request or if abuse, misuse, or diversion is suspected.
- Discuss early refill requests or other patient incidents with the prescriber so that the prescriber can make a decision to allow or deny the early refill, or to take some other action based on the patient's behavior and history.
- Report all *RMRs* to the LUMRYZ REMS by completing and submitting the *RMR* online at www.LUMRYZREMS.com or by fax to 1-877-206-3198.
- Determine whether an alert should be placed in the patient's profile in the patient database within the LUMRYZ REMS for repeated reports of lost, stolen, destroyed, or spilled drug for review prior to shipping LUMRYZ.
- Inform a pharmacist immediately if certified pharmacy staff suspects patients or prescribers of abuse, misuse, or diversion.

ADVERSE EVENT REPORTING

- Everyone on staff in each certified pharmacy has an essential role to play in the process of collecting information on potential adverse events for reporting to the LUMRYZ REMS.
  - Document and report all potential adverse events reported by all sources, including any CNS depression, respiratory depression, loss of consciousness, coma, and death by contacting Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335.

ONGOING PATIENT EDUCATION

Patients in the LUMRYZ REMS have access to ongoing education while taking LUMRYZ through:

- A 24-hour/7 day a week toll-free telephone help line staffed by a pharmacist trained in the LUMRYZ REMS,
- Continued contact with the certified pharmacy for every refill, and
- The LUMRYZ REMS website (www.LUMRYZREMS.com).

CERTIFIED PHARMACY TRAINING — PHARMACIST MODULE

LUMRYZ™ REMS

Training for Pharmacists Involved in the Dispensing of LUMRYZ

All LUMRYZ REMS certified pharmacy pharmacists involved in dispensing LUMRYZ must complete training on the **Pharmacist Module** (in addition to the **Pharmacy Staff Module**) and successfully complete the *Pharmacist Knowledge Assessment* and *Pharmacy Staff Knowledge Assessment*. Training must be completed annually.

Lumryz™

(sodium oxybate) for extended-release oral suspension Ⓒ

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All pharmacists involved in dispensing LUMRYZ must complete the following additional training at least annually. The LUMRYZ REMS requires that pharmacists within a certified pharmacy are thoroughly trained on the requirements of the LUMRYZ REMS. Training will be conducted by reviewing the LUMRYZ REMS materials and successfully completing the *Knowledge Assessments* on the requirements of certified pharmacies and pharmacists working within a certified pharmacy. These duties will include:

- Review of the LUMRYZ Prescribing Information.
- Review of certified pharmacy's internal processes and procedures established to support the LUMRYZ REMS with an experienced pharmacist.
- Execution of the *Patient Counseling Checklist* for new patients, existing patients who restart treatment after not receiving LUMRYZ for 6 months or longer, and patients who report a change in their medication or medical history.
- Detailed monitoring including completion of a *RMR*, as needed.
- Follow-up interactions with patients and prescribers.
- LUMRYZ REMS documentation and processes.

LUMRYZ REMS REQUIREMENTS

LUMRYZ may be prescribed and dispensed only to patients enrolled in the LUMRYZ REMS. Because of the risks of CNS depression, abuse, misuse, and diversion, LUMRYZ is available only through a restricted program called the LUMRYZ REMS.

Required components of this REMS include:

- Use of a certified pharmacy.
- Healthcare providers who prescribe LUMRYZ must complete and submit the following to the LUMRYZ REMS:
  - The *Prescriber Enrollment Form*
  - The *Patient Enrollment Form*
- Healthcare providers who prescribe LUMRYZ complete prescriptions for LUMRYZ on the *Prescription Form* and submit the completed form to a certified pharmacy.
  - Prescription refills and renewals may be conveyed by phone, fax, mail, and online through a prescribing system
- To receive LUMRYZ, patients must be:
  - Enrolled in the LUMRYZ REMS.
  - Prescribed LUMRYZ by a prescriber certified in the LUMRYZ REMS.
  - Counseled on the serious risks and safe use of LUMRYZ.
  - Have only one active oxybate product prescription.

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CERTIFIED PHARMACY RESPONSIBILITIES

Certified pharmacies will:

- Limit the first prescription fill to no more than a 1-month (30-day) supply of LUMRYZ and no more than a 3-month (90-day) supply for subsequent prescription fills.
- Report potential adverse events to Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335.
- Notify prescribers when there are signs of potential abuse or misuse or when patients are taking sedative hypnotics, other CNS depressants, or other potentially interacting agents of which the prescriber is not already aware.
- Certified pharmacies must complete and submit a *RMR* to the LUMRYZ REMS for all instances of potential abuse, misuse, or diversion.
- Utilize the LUMRYZ REMS, which has access to the secure, validated, separate and distinct LUMRYZ REMS databases (patient database, certified prescriber database, certified pharmacy database, and disenrolled prescriber database) that will only be queried independently through electronic verification, to verify the following:
  - Complete patient enrollment information
  - Complete prescriber certification information
  - Patient information including:
    - Name and two additional identifiers (date of birth, phone number, address, gender)
    - Current and previous prescribers
    - Comorbid conditions and concomitant medications reported by the patient
    - Prescription history
  - Prescription information including:
    - Date
    - Dose
    - Titration instructions (as applicable)
    - Number of refills
    - Directions
    - Total quantity (dose packets and number of days' supply)
    - Concomitant medications
  - *RMRs*
  - Shipment information, including:
    - Dates of shipments
    - Dates of shipment receipts
    - Patient addresses
    - Designee information
    - Number of shipments sent daily
    - Quantities of LUMRYZ dispensed daily
  - Documentation of interactions with prescribers, patients, and other parties

These data must be available to the LUMRYZ REMS for review on an ongoing basis to ensure that LUMRYZ is dispensed to enrolled patients only after completion and documentation of safe use conditions. In certain cases, a pharmacist must access a patient's or prescriber's historical data in the LUMRYZ REMS using the certified pharmacy secure web viewing portal for the patient database and review it prior to dispensing LUMRYZ.

PATIENT COUNSELING AND SCREENING

- Certified pharmacies must complete the *Patient Counseling Checklist* and submit to the LUMRYZ REMS prior to dispensing LUMRYZ for new patients, existing patients who restart treatment after not receiving LUMRYZ for 6 months or longer, and patients who report a change in their medication or medical history.
- For new patients (first shipment of LUMRYZ), and for patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer, the *Patient Counseling Checklist* must be completed in its entirety.
- For prescription renewals and refills, if the patient has indicated a change in their medication use or medical history, the patient will be transferred to the pharmacist to determine if further counseling and prescriber outreach is required. Steps 1, 3, 4 and 5 of the *Patient Counseling Checklist* must be completed if the patient indicates that the patient is taking a new medication or has a new comorbid medical condition that is listed in Step 4 of the *Patient Counseling Checklist*.
- Each time a pharmacist completes the *Patient Counseling Checklist*, the pharmacist must:
  - Verify that early refill requests have been thoroughly questioned and approved through the *RMR* procedure (see below).
  - Screen the patient for concomitant use of contraindicated medications (sedative hypnotics), alcohol, other CNS depressants or other potentially interacting agents.
    - The pharmacist asks the patient if he or she is taking any other medications and can consult external pharmacy databases to identify drug interactions or prescriptions for other drug products that might have been filled at different pharmacies before filling the LUMRYZ prescription.
    - If patient use of a contraindicated medication is confirmed, and if the prescriber has not indicated prior knowledge, then the pharmacist will notify and consult the prescriber about the risks of concomitant medication use prior to shipping LUMRYZ.
    - Instruct the patient to alert the pharmacy to any new medication the patient begins as soon as possible.
  - Screen the patient for other medical conditions.
    - The pharmacist asks the patient what other medical conditions he/she has.
    - If the patient indicates that he/she has a certain medical condition listed on the *Patient Counseling Checklist*, the pharmacist counsels the patient and notifies the prescriber, if there is no confirmation of prior prescriber knowledge, about the medical condition prior to shipping LUMRYZ.
  - Document the results of the patient screening, all reported concomitant medications and comorbid medical conditions, the action(s) taken, and the date the *Patient Counseling Checklist* is completed in the LUMRYZ REMS.
  - Counsel the patient on proper drug disposal if patient has unused oxybate product from a prior prescription (e.g., receiving an early refill for a dosage increase, alternative dose form of oxybate products, etc.).
  - Submit the *Patient Counseling Checklist* to the LUMRYZ REMS online at www.LUMRYZREMS.com or complete a print version and fax to the LUMRYZ REMS at 1-877-206-3198.
- Certified pharmacies must provide patients with 24/7 access to a LUMRYZ REMS trained pharmacist.

CLINICAL USAGE CLARIFICATIONS

The pharmacist must:

- Review the information on each *Prescription Form*.
- Notify and consult the prescriber if there are any clinical usage clarifications required, such as:
  - Dose over recommended dosage range (6 g to 9 g per night)
  - Non-standard doses or instructions
  - Possible errors in dosing or titration amounts or directions

If the issue is not resolved with the prescriber, the pharmacist may consult with the Pharmacist-in-Charge at his/her certified pharmacy and with the LUMRYZ REMS.

PRESCRIPTION REFILLS

- Up to 5 refills are allowed on a LUMRYZ prescription (per DEA regulations for Schedule lll controlled substances).
- Refills may be submitted from the prescriber to the certified pharmacy by phone, fax, mail, and online through a prescribing system. When the prescription information is entered into the PMS, the LUMRYZ REMS will verify eligibility and issue a PDA.
- For information on the prescription processing requirements see **Prescription Processing** – in the Pharmacy Staff Module.
- Refill orders should be opened at a patient's certified pharmacy when the patient has approximately 10 days of therapy remaining from the previous shipment.
  - Certified pharmacy staff will contact the patient and schedule a shipment. The pharmacy staff will ask the patient if there has been any change in his/her medications or medical history.
  - If the patient reports a change in their medication or medical history, the pharmacy staff will then transfer the patient to a pharmacist who must complete the *Patient Counseling Checklist*. The patient should be counseled on the use or diagnosis of:
    - Sedative hypnotics (for example, diazepam, phenobarbital, zolpidem, etc.)
    - CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating antiepileptic drugs, general anesthetics, and muscle relaxants
    - Alcohol
    - Sleep apnea
    - Asthma, COPD, or other conditions affecting his or her breathing
    - Other current medical conditions
  - The pharmacist completes refill counseling and confirmation of prescriber consultation or notification by completing and submitting the *Patient Counseling Checklist* as applicable to the LUMRYZ REMS online at www.LUMRYZREMS.com or by fax to 1-877-206-3198.
- All patient requests for early refills are to be questioned and documented by the pharmacist.
  - An early refill request is a request for LUMRYZ shipment prior to the date of the next shipment.
  - Requests to accommodate shipment logistics (scheduled delivery date falls on a Sunday, holiday, or vacation) are not considered early refills.
  - If the early refill is required due to a dosage increase, a pharmacist must:
    - Confirm the new dosage with the prescriber prior to processing the prescription.

- If an early refill is requested for any other reason, a pharmacist must:
  - Discuss the request with the patient to evaluate his/her compliance with therapy, assessing for misuse, abuse, and diversion.
  - Evaluate the patient's record in the LUMRYZ REMS using the certified pharmacy secure web viewing portal for the patient database and review the patient's prior *RMR* history to identify previous reports of early refills or other incidents suggestive of abuse, misuse, and diversion.
  - Contact the prescriber to discuss the request and any prior early refill requests or incidents suggestive of abuse, misuse, and diversion.
  - Send new shipments of LUMRYZ to the patient only if approved by the prescriber.
  - Send new shipments to replace LUMRYZ reported stolen by a patient only after obtaining a copy of the police report filed by the patient.
  - Document the discussion and outcome by completing and submitting the *RMR* to the LUMRYZ REMS online at www.LUMRYZREMS.com or by fax to 1-877-206-3198.

MONITORING AND ASSESSING FOR SIGNS OF ABUSE, MISUSE, AND DIVERSION

- Risk management events must be documented in the LUMRYZ REMS.
  - Risk management events are reported or discovered events outside the norm that give rise to a reasonable suspicion of abuse, misuse, or diversion.
  - Examples of events that should generate a *RMR* include but are not limited to:
    - Requests for early refills
    - Patient's misuse or abuse of product
    - Lost, stolen, destroyed, or spilled drug
    - Delivery to incorrect address and not returned
    - Patient claims that product was not delivered while carrier shows receipt of delivery
    - Product tampering
    - Counterfeit product
    - Contaminated product
    - Inquiries and/or arrests by law or regulatory enforcement agencies associated with the misuse, abuse, or diversion of the product
    - Crimes related to the product
  - *RMRs* must document:
    - Patient and/or prescriber identifying information
    - Reason for report
    - Certified Pharmacy actions
    - Prescriber contact
    - Supporting documentation (if applicable, such as a police report, fire report, DEA Form 106, or shipper investigation report)
  - Pharmacies can request that a patient be monitored by the LUMRYZ REMS if serious or repeated events give rise to reasonable suspicion of misuse, abuse or diversion.
  - If abuse, misuse, or diversion is suspected, the pharmacist must review the patient's *RMR* history and discuss the incident with the prescriber prior to shipping LUMRYZ.
  - Repeated reports of lost, stolen, destroyed, or spilled drug will be documented as an alert to the patient record

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stored in the patient database of the LUMRYZ REMS and will be accessible to the dispensing pharmacist using the secure web viewing portal for the patient database for review prior to shipping drug.

- Certified pharmacies and/or prescribers may request the LUMRYZ REMS to disenroll a patient after review and discussion of incidents suggestive of abuse, misuse, or diversion by completing and submitting a *RMR* to the LUMRYZ REMS. All requests from prescribers to disenroll a patient will be reported to a certified pharmacy. The certified pharmacy is required to intake the request, then complete and submit the *RMR* to the LUMRYZ REMS to request disenrollment. Avadel CNS Pharmaceuticals, LLC will review the information and determine if the patient should be disenrolled.
- Pharmacies may recommend that a prescriber be disenrolled by submitting a *RMR* to the LUMRYZ REMS. Avadel CNS Pharmaceuticals, LLC will review the information and determine if the prescriber should be disenrolled.
- All *RMRs* must be reported to the LUMRYZ REMS online at www.LUMRYZREMS.com or by fax to 1-877-206-3198.

SHIPPING PROCEDURES

- LUMRYZ must be shipped via an overnight service with receipt signature required.
  - LUMRYZ is shipped directly to the patient or adult designee (18 years, or 21 years if required by carrier) if the patient is not available to receive the order.
- The patient may request an alternate shipping address, which is then subject to approval by a pharmacist.
- If the patient requests Saturday delivery, his/her certified pharmacy will verify with the overnight shipping service that Saturday delivery is available for the shipping address.
- Each LUMRYZ shipment must include:
  - A carton with the prescribed amount of LUMRYZ packets at the prescribed dose (each child-resistant packet contains a single dose of LUMRYZ 4.5 g, 6 g, 7.5 g, or 9 g).
  - A mixing cup for preparation of each single dose (LUMRYZ dose mixed with water).
  - The *Patient Brochure* (new patients only).
- Daily tracking reports must be generated by each certified pharmacy to confirm the receipt of each order shipped during the previous 48 hours. Saturday deliveries are confirmed the following Monday.
  - A patient will be contacted if there is no proof of patient or designee signature, if the patient or designee on file did not sign for the shipment, or if there is a potential incomplete delivery.
  - If a shipment is reported lost, an investigation will be launched to find it.
  - Receipt of each shipment of LUMRYZ by a patient must be reported to the LUMRYZ REMS by the patient's certified pharmacy electronically, through the website (www.LUMRYZREMS.com), or by calling (1-877-453-1029).

INVENTORY CONTROL

The LUMRYZ inventory must be reconciled every two weeks and recorded in the pharmacy management system. A physical count must match the count in the pharmacy management system. If the LUMRYZ inventory cannot be reconciled, no other patient orders can be processed until an investigation is completed and approved by the Pharmacist in Charge. Documentation must be made available in the event of an audit.

LUMRYZ™ REMS | Pharmacy Staff Knowledge Assessment

Lumryz.
(sodium oxybate) for extended-release oral suspension

For immediate processing, please go to www.LUMRYZREMS.com.

To submit this form via fax, please complete all required fields below and fax to 1-877-206-3198. You will receive a confirmation of your successful completion of the Knowledge Assessment via email.

PHARMACY STAFF INFORMATION

(*denotes required field)

*First Name:	*Last Name:	
*Phone:	*Fax:	*Email:
*Pharmacy Name:		
NCPDP No.:	*NPI No.:	

LUMRYZ REMS TRAINING: PHARMACY STAFF MODULE

SELECT THE BEST ANSWER FOR EACH OF THE FOLLOWING QUESTIONS.

1. LUMRYZ (sodium oxybate) for extended-release oral suspension is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.
   A. True B. False

2. LUMRYZ contains the sodium salt of gamma-hydroxybutyrate (GHB) and is a controlled substance because:
   A. It can make the patient sleepy quickly
   B. It must be taken while in bed
   C. It has abuse and misuse potential
   D. It requires preparing a suspension before dosing

3. LUMRYZ is contraindicated in patients who:
   A. Take sedative hypnotics
   B. Drink alcohol while using LUMRYZ
   C. Have succinic semialdehyde dehydrogenase deficiency, a rare disorder of inborn error of metabolism variably characterized by mental retardation, hypotonia, and ataxia
   D. All of the above

4. Healthcare providers should caution patients about operating hazardous machinery for at least six (6) hours after taking a dose of LUMRYZ.
   A. True B. False

5. The LUMRYZ REMS has which of the following requirements?
   A. Use of a limited number of certified pharmacies
   B. Healthcare providers who prescribe LUMRYZ must be certified in the REMS and must comply with the requirements of the LUMRYZ REMS
   C. For patients to receive LUMRYZ, they must be enrolled in the LUMRYZ REMS and be counseled on the serious risks and safe use of LUMRYZ
   D. All of the above

6. In processing enrollment information, the LUMRYZ REMS requires all of the following EXCEPT:
   A. Confirmation that the prescriber's DEA, state license, and NPI numbers are active and the prescriber has provided all REMS-related attestation
   B. Maintaining enrollment form information in the appropriate LUMRYZ REMS database
   C. Searching the patient database to determine if a patient is already enrolled (duplicate patient)
   D. Ensuring refill orders are shipped when a patient has approximately 10 days of therapy remaining from the previous shipment
   E. Disenrolling a patient or prescriber for noncompliance with the LUMRYZ REMS requirements

7. In validating a prescription for LUMRYZ, the certified pharmacy will verify that:
   - The *Prescription Form* is complete and signed by the prescriber
   - The prescription is dated according to state-controlled substance regulations
   - The prescription is for no more than a 1-month (30-day) supply on a patient's first LUMRYZ fill and no more than a 3-month (90-day) supply on subsequent fills
   - There are no discrepancies or concerns with dosing and titration
   - A pre-dispense authorization (PDA) from the LUMRYZ REMS has been obtained to confirm the prescriber is certified, the patient is enrolled, the patient has no other active LUMRYZ prescriptions, and the pharmacy confirmed phone calls to the other REMS for oxybate products to verify the patient has no other active, overlapping prescription for oxybate products that overlap with the current prescription for LUMRYZ and that the patient and prescriber has not been disenrolled from any other REMS for oxybate products for suspected abuse, misuse, or diversion were completed

   A. True B. False

8. A certified pharmacy must not stock LUMRYZ in retail pharmacies.
   A. True B. False

9. In monitoring patients and prescribers for signs of inappropriate prescribing, abuse, misuse, and diversion, the certified pharmacy staff will:
   A. Document early refill requests and instances of patient and prescriber behavior that suggest potential abuse, misuse, or diversion by completing a *Risk Management Report (RMR)*
   B. Review the patient's *RMR* history and alerts in the LUMRYZ REMS
   C. Inform a pharmacist immediately if certified pharmacy staff suspects a patient or prescriber of abuse, misuse, or diversion
   D. Determine whether an alert should be placed in the patient's profile in the patient database within the LUMRYZ REMS
   E. All of the above

10. Certified pharmacy staff must report all potential adverse events reported by all sources including any CNS depression, respiratory depression, loss of consciousness, coma, and death to Avadel CNS Pharmaceuticals, LLC
    A. True B. False

Avadel

Reference ID: 5166429

LUMRYZ™ REMS | Pharmacist Knowledge Assessment

Lumryz.
(sodium oxybate) for extended-release oral suspension C

For immediate processing, please go to www.LUMRYZREMS.com.

To submit this form via fax, please complete all required fields below and fax to 1-877-206-3198. You will receive a confirmation of your successful completion of the Knowledge Assessment via email.

PHARMACIST INFORMATION

(*denotes required field)

*First Name:	*Last Name:	
*Phone:	*Fax:	*Email:
*Pharmacy Name:		
NCPDP No.:	*NPI No.:	

LUMRYZ REMS TRAINING: PHARMACISTS MODULE

SELECT THE BEST ANSWER FOR EACH OF THE FOLLOWING QUESTIONS.

1. Prior to dispensing LUMRYZ to a patient, the certified pharmacy will process all LUMRYZ prescriptions, regardless of payment method, through the pharmacy management system and obtain a pre-dispense authorization (PDA) via electronic verification to verify the prescriber is certified, the patient is enrolled and the patient has no other active, overlapping LUMRYZ prescriptions
   A. True B. False
2. Certified pharmacies must reconcile LUMRYZ inventory every two weeks and record in the pharmacy management system. Documentation must be made available in the event of an audit.
   A. True B. False
3. Certified pharmacies in the LUMRYZ REMS will:
   A. Limit the patient's first prescription fill of LUMRYZ to no more than a one-month (30-day) supply and subsequent prescription fills to no more than a three-month (90-day) supply
   B. Report potential adverse events to Avadel CNS Pharmaceuticals, LLC
   C. Notify prescribers when there are signs of potential abuse or misuse or when patients are taking sedative hypnotics, other CNS depressants, or other potentially interacting agents of which the prescriber is not already aware
   D. All of the above
4. Certified pharmacies in the LUMRYZ REMS must perform all of the following EXCEPT:
   A. Validate all prescriptions prior to dispensing LUMRYZ
   B. Counsel the patient by completing the *Patient Counseling Checklist* prior to dispensing LUMRYZ to new patients, existing patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer, and patients who report a change in their medication or medical history
   C. Contact the patient's prescriber prior to every dispense of LUMRYZ
   D. Monitor patients and prescribers for signs of inappropriate prescribing, abuse, misuse, and diversion and complete a *Risk Management Report Form* if needed
5. If there are clinical usage clarifications needed for a prescription, the pharmacist will:
   A. Refuse to fill the prescription
   B. Notify and consult the patient's prescriber
   C. Fill out a *Risk Management Report Form*
   D. Disenroll the prescriber
6. Which of the following is NOT true for the prescription refill process?
   A. Up to 5 refills are allowed on a LUMRYZ prescription
   B. Patient counseling must be completed and submitted to the REMS using the *Patient Counseling Checklist* if the patient reports a change in their medication or medical history
   C. Refill orders should be opened when the patient has approximately 10 days of therapy remaining from the previous shipment
   D. All refills must be countersigned by the prescriber
7. If the pharmacist identifies the patient is taking a potentially interacting agent that may present a risk to the patient, the pharmacist should consider which of the following actions before filling the prescription?
   A. Notifying law enforcement
   B. Taking no action
   C. Consulting with the patient's prescriber
   D. Consulting with the patient's insurance provider
8. In monitoring and assessing for signs of abuse, misuse, or diversion, a pharmacist should complete a *Risk Management Report Form* for which of the following events?
   A. Early refill requests (excluding requests to accommodate shipment logistics)
   B. Lost, stolen, destroyed, or spilled drug
   C. Patient claims that product was not delivered while carrier shows receipt of delivery
   D. Patient's misuse or abuse of product
   E. All of the above
9. Each shipment of LUMRYZ must include:
   - A carton with the prescribed amount of LUMRYZ packets at the prescribed dose (each child-resistant packet contains LUMRYZ 4.5 g, 6 g, 7.5 g, or 9 g)
   - A mixing cup for preparation of each single dose (LUMRYZ dose mixed with water)
   - A *Patient Brochure* (new patients only)

   A. True B. False
10. All LUMRYZ prescriptions must be shipped to the patient or adult designee via:
    A. Certified mail with receipt signature
    B. Overnight service with receipt signature required
    C. Medical courier
    D. United States Postal Service with delivery receipt

Reference ID: 5166429

LUMRYZ™ REMS | LUMRYZ Prescription Form

LUMRYZ (sodium oxybate) for extended-release oral suspension

Lumryz. (sodium oxybate) for extended-release oral suspension ©

Fax completed form to one of the certified pharmacies.

A list of certified pharmacies is available to certified prescribers at www.LUMRYZREMS.com or by calling the LUMRYZ REMS at 1-877-453-1029.
For more information, please call the LUMRYZ REMS at 1-877-453-1029.

Note: This form may not satisfy all legal requirements for prescribing LUMRYZ in your state.
Please submit all prescriptions in accordance with applicable state laws or as required by institutional policy. Please Print (*denotes required field)

PRESCRIBER INFORMATION

*First Name:	M.I.:	*Last Name:	
*NPI No.:	*DEA No.:	*State License No.:	
*Street Address:		*Phone:	
*City:	*State:	*Zip Code:	*Fax:
Office Contact Name:		Office Contact Phone:	

PATIENT INFORMATION

*First Name:	M.I.:	*Last Name:	*Primary Phone:
*Date of Birth (MM/DD/YYYY):	*Gender: ☐ Male ☐ Female ☐ Other		Cell Phone:
*Address:			Work Phone:
*City:	*State:	*Zip Code:	Email:

***Medications:** (list all known current prescription and non-prescription medications and dosages or submit as a separate page)
☐ Check box if separate page(s) attached. Total number of additional pages: _____

Comorbidities: (list all known comorbidities or submit as a separate page)
☐ Check box if separate page(s) attached. Total number of additional pages: _____

LUMRYZ PRESCRIPTION

_____ LUMRYZ 4.5 g 7 dose packets QTY: _____ box(es) of 7
_____ LUMRYZ 6 g 7 dose packets QTY: _____ box(es) of 7
_____ LUMRYZ 7.5 g 7 dose packets QTY: _____ box(es) of 7
_____ LUMRYZ 9 g 7 dose packets QTY: _____ box(es) of 7
*Only one strength shipped to patient at a time

_____ LUMRYZ 4.5 g 30 dose packets QTY: _____ box(es) of 30 _____ refills
_____ LUMRYZ 6 g 30 dose packets QTY: _____ box(es) of 30 _____ refills
_____ LUMRYZ 7.5 g 30 dose packets QTY: _____ box(es) of 30 _____ refills
_____ LUMRYZ 9 g 30 dose packets QTY: _____ box(es) of 30 _____ refills
*Only one strength shipped to patient at a time

DISPENSING INSTRUCTIONS

Initial prescription fill cannot exceed 1 month of therapy; refills cannot exceed 3 months' supply of therapy.

Directions: Take contents of one packet mixed with water in provided mixing cup at bedtime.
Note: Prepare the dose of LUMRYZ at bedtime according to label instructions. The LUMRYZ shipment does not include water for mixing.

Special Instructions:

PRESCRIBER VERIFICATION – My signature below signifies that: I understand the statements and agree to the LUMRYZ REMS requirements which are found on page 2 of this form; LUMRYZ is medically appropriate for this patient; and, I have informed the patient that the LUMRYZ REMS will send him/her a *Patient Brochure* with his or her first prescription fill.

_____ *Prescriber Signature

_____ *Date

Printed Supervising Physician Name (if required by state law):

_____ Supervising Physician Signature

_____ Date

PHARMACY VERIFICATION – My signature below signifies that: I understand the statements and agree to the LUMRYZ REMS requirements which are found on page 2 of this form.

_____ *Pharmacist Signature

_____ *Date

Avadel

Lumryz
(sodium oxybate) for extended-release oral suspension ℄

Prescriber and Pharmacist: Signature verification is required on the first page of this *Prescription Form* as acknowledgment that you have an understanding of and/or agree to the following:

PRESCRIBER ATTESTATIONS

I understand that:

- LUMRYZ is approved for the treatment of
  - Cataplexy in adults with narcolepsy.
  - Excessive daytime sleepiness (EDS) in adults with narcolepsy.
- LUMRYZ is a Schedule III central nervous system (CNS) depressant and can cause obtundation and clinically significant respiratory depression at recommended doses.
- LUMRYZ is contraindicated in combination with alcohol and sedative hypnotics.
- Concurrent use of LUMRYZ with certain 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.
- Patients who have sleep apnea or compromised respiratory function (e.g., asthma, COPD, etc.) may be at higher risk of developing respiratory depression, loss of consciousness, coma, and death with LUMRYZ use.

I have read and understand the Prescribing Information and *Prescriber Brochure*.

I have screened this patient for:

- History of alcohol or substance abuse, sleep-related breathing disorders, compromised respiratory function, depression or suicidality, concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents.

I have counseled this patient on:

- The serious risks and safe use, handling, and storage of LUMRYZ using the *Patient Brochure*.

Before treatment re-initiation, I must:

- **For patients disenrolled for suspicion of abuse, misuse, or diversion:** Communicate with the pharmacy regarding all relevant patient history and re-enroll the patient if the pharmacist and I agree.
- **For patients with a lapse in treatment of 6 months or longer:** Order LUMRYZ using the *Prescription Form* and submit it to a certified pharmacy.

Within the first 3 months of starting treatment, I must:

- Assess the patient for:
  - Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents
  - Serious adverse events
  - Signs of abuse and misuse, including an increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, and/or drug-seeking behavior

It is recommended that patients be re-assessed every 3 months while taking LUMRYZ.

I must:

- Report potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Avadel CNS Pharmaceuticals, LLC.
- Report requests to disenroll a patient to a certified pharmacy.

PHARMACIST ATTESTATIONS

As the pharmacist, I must

- Verify that the patient has no other active, overlapping prescriptions for an oxybate product that overlap with the current LUMRYZ prescription.
- Verify the patient and prescriber have not been disenrolled in the other REMS for oxybate products for suspected abuse, misuse, or diversion.
- Report this prescription filled for LUMRYZ to the LUMRYZ REMS and the other REMS for oxybate products.

LUMRYZ™ REMS | Patient Counseling Checklist

Lumryz
(sodium oxybate) for extended-release oral suspension C

To be completed by the pharmacist online at www.LUMRYZREMS.com
or
by printing and faxing the completed form to the LUMRYZ REMS at 1-877-206-3198 prior to dispensing LUMRYZ to new patients, existing patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer, and patients who report a change in their medication or medical history. Include additional requirements (if any) per federal or state requirements that need to be collected as part of the patient counseling process.

PHARMACIST INFORMATION (All fields required)

Pharmacist First Name:	Pharmacist Last Name:
Phone:	Email.:
Pharmacy Name:	NPI No.:

PATIENT INFORMATION (All fields required)

First Name:	Last Name:
Date of Birth (MM/DD/YYYY):	REMS ID Number:

ALL STEPS BELOW ARE REQUIRED AND MUST BE COMPLETED BY CHECKING THE BOXES AND INITIALING/DATING THE BOTTOM OF EACH PAGE.

STEP 1: PATIENT INFORMATION (Select One)

(Complete this section for new patients (first shipment of LUMRYZ), existing patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer, and patients who report a change in their medication use or medical history listed in Step 4 of this checklist)

- ☐ New/restart
- ☐ Scheduled refill
- ☐ Early refill approved through *Risk Management Report (RMR)* process

STEP 2: COUNSELING

(Complete this section for new patients (first shipment of LUMRYZ) and existing patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer)

- ☐ Verify that the patient will receive the *Patient Brochure.*
- ☐ Verify that the patient has been counseled on **Therapy Expectations** below:
  - During clinical trials with LUMRYZ, many patients with narcolepsy saw some improvement with excessive daytime sleepiness and/or cataplexy in the first weeks after beginning LUMRYZ therapy. However, the response to LUMRYZ can vary from patient to patient. It may also take time to find the right dose that works for you. Your doctor will determine the dose that is appropriate for you.
  - Be sure to talk to your doctor about any troubling side effects or if you don't feel any benefits while taking LUMRYZ.
  - For any changes to your prescription, have your doctor call or fax the new prescription change to the pharmacy. NEVER attempt to change the dose yourself.
- ☐ Verify that the patient has been counseled on **Preparation and Administration** information below:
  - LUMRYZ should be taken as directed by your doctor (review prescriber's instructions with patient).
  - LUMRYZ should be taken at least 2 hours after eating.
  - Prepare your dose of LUMRYZ as follows:
    - Before going to bed, gather the following supplies and place them on a flat surface at your bedside:
      - 1 bottle or glass of water (1/3 cup). Do not use hot water;
      - 1 LUMRYZ packet from the carton;
      - 1 clean mixing cup; and
      - 1 pair of scissors (optional).
    - Fill the mixing cup with water up to Fill Line A (top line) and set the mixing cup on a flat surface at your bedside.
    - Open one LUMRYZ packet (by either tearing at the tear mark or cutting with scissors) and pour the entire content from the packet into the water-filled mixing cup.
    - Place the cap on the mixing cup and shake well for at least 60 seconds (1 minute). The mixed solution should appear slightly milky and may contain some lumps. Make sure to drink all the mixed solution in the mixing cup.
    - Immediately after drinking the mixed solution, refill the mixing cup with water up to Fill Line B (lower line) to mix in any medicine left in the mixing cup.
    - Place the cap on the mixing cup and shake well for at least 10 seconds. Again, while in bed, make sure to drink all the mixed solution in the mixing cup within 30 minutes of mixing. If not taken within 30 minutes of mixing, throw it away (dispose of it) and prepare a new dose.
    - Leave the empty mixing cup at your bedside and immediately lie down to go to sleep. Avoid getting out of bed after taking LUMRYZ.

Pharmacist Initials: _____ Date (mm/dd/yyyy): _____

Lumryz.
(sodium oxybate) for extended-release oral suspension ©

- Refer to the LUMRYZ Medication Guide for additional information on preparation of your LUMRYZ dose.
- Feel free to call your certified pharmacy if you have any questions about preparing your dose or how to take your LUMRYZ doses. The LUMRYZ REMS is also available Monday through Friday, from 8 am to 8 pm Eastern Time, at 877-453-1029, and a pharmacist is always available 24 hours a day, 7 days a week at your certified pharmacy, if needed.
- Patients usually fall asleep in about 5 to 15 minutes, although some patients have reported falling asleep more quickly (without first feeling drowsy) and others may take longer to fall asleep. The time it takes to fall asleep might be different from night to night.
- Be sure to store LUMRYZ in the original carton in a safe and secure place out of the reach of children and pets. Get emergency help (call 911) right away if a child ingests LUMRYZ.
- LUMRYZ should be stored at room temperature.

Note to pharmacist: If patient has unused sodium oxybate from a prior prescription (e.g., receiving an early refill for a dosage increase, alternative dose form of sodium oxybate), counsel the patient on proper drug disposal.

☐ Verify that the patient has been counseled on **Precautions Needed for LUMRYZ Use** below:

- LUMRYZ is classified as a controlled substance medication. LUMRYZ must be used only by the person for whom it is prescribed and as directed by the prescriber. All lost or stolen medication must be reported to local police and your pharmacy.
- Federal law prohibits the transfer of LUMRYZ to any person other than the patient for whom it was prescribed.
- LUMRYZ is sodium oxybate. The active ingredient in sodium oxybate is gamma-hydroxybutyrate (GHB), which is associated with serious adverse reactions with illicit use and abuse.
- Abuse of GHB can lead to dependence (a physical need to take the drug), craving for the medicine, and severe withdrawal symptoms (symptoms that start when the drug is stopped, especially when it is stopped suddenly). Abuse of GHB, with or without other CNS depressants (for example, nortriptyline, oxycodone, or heroin) including alcohol can lead to seizure, trouble breathing, decreases in the level of consciousness, coma, and death.
- Tell your doctor if you:
  - Are pregnant or plan to become pregnant. It is not known if LUMRYZ can harm your unborn baby.
  - Are breastfeeding or plan to breastfeed. LUMRYZ passes into breast milk. You and your doctor should decide if you will take LUMRYZ or breastfeed.
  - Have or had depression or tried to harm yourself. You should be watched carefully for new symptoms of depression.
  - Have liver problems.
  - Have short periods of not breathing while you sleep (sleep apnea), snoring, trouble breathing, or lung problems. You may have a higher chance of serious breathing problems with LUMRYZ.
  - Have mental health problems.
  - Have experienced sleepwalking.
  - Are on a salt-restricted diet, have high blood pressure, heart failure, or kidney problems. LUMRYZ contains sodium (salt) and may not be right for you.

☐ Verify that the patient has been counseled on **Side Effects** below:

- In the placebo-controlled clinical trial for LUMRYZ, the most common adverse reactions reported for any dose of LUMRYZ were nausea, dizziness, enuresis (bedwetting), headache, and vomiting.
- LUMRYZ can cause serious side effects, including trouble breathing while sleeping, confusion, unusual or disturbing thoughts, depression, thoughts of killing yourself or trying to kill yourself, and sleepwalking, even at recommended doses. Tell your doctor if you have any of these problems while taking LUMRYZ.
- Remember that you must not drive a car, operate heavy machinery, or perform any activity that is dangerous or that requires mental alertness or motor coordination for at least 6 hours after taking LUMRYZ.
- When taking LUMRYZ, do not drink alcohol or take medicines that make you sleepy unless specifically prescribed by your doctor for use with LUMRYZ, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating antiepileptic drugs, general anesthetics, muscle relaxants, and/or illicit CNS depressants.
- These are not all of the side effects that you might experience. Contact your doctor if you are concerned about any possible side effects. Refer to the LUMRYZ Medication Guide for additional information on possible side effects.

Pharmacist Initials: _____ Date (mm/dd/yyyy): _____

Phone: 1-877-453-1029 | www.LUMRYZREMS.com | Fax: 1-877-206-3198

Lumryz.
(sodium oxybate) for extended-release oral suspension ℂ

STEP 3: SCREENING

(Complete this section for new patients (first shipment of LUMRYZ), existing patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer, and patients who report a change in their medication or medical history listed in Step 4 of this checklist)

1. Is the patient taking sedative hypnotics (for example, eszopiclone, zaleplon, zolpidem, temazepam, suvorexant, quazepam, estazolam, flurazepam, triazolam, tasimelteon, ramelteon)?

☐ Yes ☐ No If Yes, ☐ Counseled Patient

Please list the drug(s) and dose of each:	Drug	Dose

2. Is the patient taking benzodiazepines (for example, diazepam, alprazolam or any not listed in question 1), sedating antidepressants or antipsychotics, sedating antiepileptics, general anesthetics, muscle relaxants, opioid analgesics, or illicit CNS depressants (for example, heroin, GHB, etc.)?

☐ Yes ☐ No If Yes, ☐ Counseled Patient

Please list the drug(s) and dose of each:	Drug	Dose

3. What other prescription and non-prescription medications is the patient taking?

Please list the drug(s) and dose of each:	Drug	Dose

4. Does the patient drink alcohol? ☐ Yes ☐ No If Yes, ☐ Counseled Patient

5. Has the patient been diagnosed with sleep apnea (short periods of not breathing while asleep)? ☐ Yes ☐ No If Yes, ☐ Counseled Patient

6. Does the patient have a diagnosis of or suffer from asthma, COPD, or other conditions affecting his/her breathing (slower breathing, trouble breathing)?

☐ Yes ☐ No If Yes, ☐ Counseled Patient

Please list the drug(s) used to treat and dose of each, if known:	Drug	Dose

7. Does the patient have any other current medical/psychiatric conditions for which the patient is under a healthcare provider's care?

☐ Yes ☐ No If Yes, ☐ Counseled Patient

Please list the condition(s), if known:	Condition

8. Does the patient have any clinical questions about LUMRYZ?

☐ Yes ☐ No If Yes, ☐ Counseled Patient **and/or** ☐ Referred Patient to Prescriber

Please list the question(s):	Question

Pharmacist Initials: _____ Date (mm/dd/yyyy): _____

Phone: 1-877-453-1029 | www.LUMRYZREMS.com | Fax: 1-877-206-3198

Avadel

Lumryz.
(sodium oxybate) for extended-release oral suspension ©

STEP 4: CONCOMITANT MEDICATION & COMORBIDITY SUMMARY

(Complete this section for new patients (first shipment of LUMRYZ), existing patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer, and patients who report a change in their medication or medical history listed in this step of this checklist)

Medication Type:

- ☐ Sedative hypnotics
- ☐ Benzodiazepines
- ☐ Alcohol
- ☐ Sedating antidepressants, antipsychotics, or antiepileptics
- ☐ General anesthetics
- ☐ Muscle relaxants
- ☐ Opioid analgesics
- ☐ Illicit CNS depressants (e.g., heroin, GHB, etc.)

Medical Conditions:

- ☐ Sleep apnea
- ☐ Asthma
- ☐ COPD
- ☐ Other conditions affecting their breathing
- ☐ History of depression and suicidality
- ☐ History of alcohol and drug abuse
- ☐ Seizure disorders
- ☐ Hepatic impairment
- ☐ High blood pressure, heart problems, kidney problems, or are on a salt-restricted diet

If any of the medication types or medical conditions listed above are checked, or any of the questions in Step 3 were answered yes and there is no confirmation of prior prescriber knowledge, call the prescriber to consult:

Is a prescriber consult required? ☐ Yes ☐ No

If no, please provide reason:_____

_____

If yes, action(s) taken (check all that apply and document details in "Prescriber consult outcome" section below):

☐ Contacted prescriber: _____/_____/_____ (Date - mm/dd/yyyy) ☐ Other: _____/_____/_____ (Date - mm/dd/yyyy)

Is prescriber consult due to concomitant sedative hypnotics or benzodiazepines?

If yes, complete all of the following questions at the conclusion of the consult. If no, complete step 5 only. ☐ No ☐ Yes

If yes, is treatment with LUMRYZ to be continued? ☐ No ☐ Yes

If yes, what action will be taken? (select one):

- ☐ Concomitant medication will be discontinued
- ☐ Dosage of concomitant medication has been/will be reduced
- ☐ No action (continue concomitant medication with LUMRYZ)
  - Prescriber's rationale for continuing concomitant medication with LUMRYZ (select one):
    - ☐ Medication will not be taken at the same time as LUMRYZ
    - ☐ Medication will be taken at the same time as LUMRYZ (select one):
      - ☐ Medication will be taken as a sleep aid
      - ☐ Medication will be taken for a different indication per medical need
      - ☐ Information unavailable
    - ☐ LUMRYZ dose regimen changed
    - ☐ No rationale provided or Information unavailable

CONSULTING PRESCRIBER INFORMATION

First Name:	Last Name:	
Prescriber Identifier (provide at least one):	NPI:	DEA:

Overall Prescriber consult outcome:_____

_____

_____

Pharmacist Initials: _____ Date (mm/dd/yyyy): _____

Phone: 1-877-453-1029 | www.LUMRYZREMS.com | Fax: 1-877-206-3198

Avadel

Lumryz.
(sodium oxybate) for extended-release oral suspension C

STEP 5: COMPLETION SUMMARY

(Complete this section for new patients (first shipment of LUMRYZ), existing patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer, and patients who report a change in their medication or medical history listed in Step 4 of this checklist)

Checklist Completed: ☐ Yes ☐ No (LUMRYZ cannot be dispensed until checklist is completed.)

If yes, date checklist completed (mm/dd/yyyy): _____/_____/_____

If no, document the reason for non-completion: _____

_____

_____

My signature below signifies:

- I understand the counseling requirements of the LUMRYZ REMS and have counseled the patient using this *Patient Counseling Checklist.*
- I will submit this checklist to the LUMRYZ REMS.

_____ _____

Pharmacist Signature **Date**

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Lumryz™
(sodium oxybate) for extended-release oral suspension

SUBJECT:
- **Serious Risks with Use of LUMRYZ™ (sodium oxybate) for extended-release oral suspension:**
  - **Central Nervous System (CNS) Depression**
  - **Abuse and Misuse**
- **FDA Required LUMRYZ REMS**

FDA-REQUIRED REMS SAFETY INFORMATION

Dear Healthcare Provider:

This letter is to inform you about the risks of CNS depression, abuse and misuse associated with LUMRYZ and the LUMRYZ REMS. LUMRYZ is a new once-at-bedtime therapy indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.

The U.S. Food and Drug Administration (FDA) has determined that a **Risk Evaluation and Mitigation Strategy (REMS)** is necessary to manage the risks of CNS depression, abuse, and misuse. LUMRYZ is only available through a restricted distribution program called the LUMRYZ REMS.

Risks of LUMRYZ

- Serious adverse outcomes from inappropriate prescribing, misuse, abuse and diversion
- Significant central nervous system (CNS) and respiratory depression
- Contraindication of use of LUMRYZ with sedative hypnotics or alcohol

LUMRYZ REMS Requirements

- Prescribers of LUMRYZ must be certified in the LUMRYZ REMS in order to prescribe LUMRYZ.
- Additional details about the requirements of the LUMRYZ REMS are outlined in the *Fact Sheet* included with this letter.
- To certify in the LUMRYZ REMS, visit www.LUMRYZREMS.com.

For additional details about the REMS, visit www.LUMRYZREMS.com or contact the LUMRYZ REMS at 1-877-453-1029.

The information in this letter is not intended as a complete description of the benefits and risks associated with the use of LUMRYZ. Please see the accompanying Prescribing Information including the Medication Guide.

Adverse Event Reporting

Report serious adverse events of LUMRYZ to Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335 and/or the FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).

Sincerely,

Avadel CNS Pharmaceuticals, LLC

Lumryz™
(sodium oxybate) for extended-release oral suspension

SUBJECT:
- **Serious Risks with Use of LUMRYZ™ (sodium oxybate) for extended-release oral suspension:**
  - **Central Nervous System (CNS) Depression**
  - **Abuse and Misuse**
- **FDA Required LUMRYZ REMS**

FDA-REQUIRED REMS SAFETY INFORMATION

Dear Professional Society:

We request that you share the following with your members.

This letter is to inform prescribers about the risks of CNS depression, abuse and misuse associated with LUMRYZ and the LUMRYZ REMS. LUMRYZ is a new once-at-bedtime therapy indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.

The U.S. Food and Drug Administration (FDA) has determined that a **Risk Evaluation and Mitigation Strategy (REMS)** is necessary to manage the risks of CNS depression, abuse, and misuse. LUMRYZ is only available through a restricted distribution program called the LUMRYZ REMS.

Risks of LUMRYZ

- Serious adverse outcomes from inappropriate prescribing, misuse, abuse and diversion
- Significant central nervous system (CNS) and respiratory depression
- Contraindication of use of LUMRYZ with sedative hypnotics or alcohol

LUMRYZ REMS Requirements for Prescribers

- Prescribers of LUMRYZ must be certified in the LUMRYZ REMS in order to prescribe LUMRYZ.
- Additional details about the requirements of the LUMRYZ REMS are outlined in the *Fact Sheet* included with this letter.
- To certify in the LUMRYZ REMS, prescribers should visit www.LUMRYZREMS.com.

For additional details about the REMS, visit www.LUMRYZREMS.com or contact the LUMRYZ REMS at 1-877-453-1029.

The information in this letter is not intended as a complete description of the benefits and risks associated with the use of LUMRYZ. Please see the accompanying Prescribing Information including the Medication Guide.

Adverse Event Reporting

Prescribers are to report serious adverse events of LUMRYZ to Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335 and/or the FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).

Sincerely,

Avadel CNS Pharmaceuticals, LLC

Lumryz.
(sodium oxybate) for extended-release oral suspension

LUMRYZ™ REMS Fact Sheet

LUMRYZ REMS OVERVIEW

What is the LUMRYZ REMS (Risk Evaluation and Mitigation Strategy)?

The LUMRYZ REMS is a safety program that manages the risk of serious adverse outcomes from inappropriate prescribing, misuse, abuse, and diversion of LUMRYZ. The LUMRYZ REMS is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks. The LUMRYZ REMS is a restricted distribution program.

PRESCRIBERS must be certified in the LUMRYZ REMS

PHARMACIES must be certified in the LUMRYZ REMS as well as verify that prescribers are certified, and patients are authorized to receive LUMRYZ

PATIENTS must be enrolled in the LUMRYZ REMS

Scan to access

WHAT IS THE RISK?

LUMRYZ:

- Is a central nervous system (CNS) depressant and can cause obtundation and clinically significant respiratory depression at recommended doses
- Has a known potential for abuse and misuse, 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

How Can Prescribers Manage the Risk?

- Screen each patient for history of alcohol, drug abuse, sleep-related breathing disorders, compromised respiratory function, depression, suicidality, concomitant use of sedative hypnotics, other CNS depressants or other potentially interacting agents
- Counsel each patient prior to initiating therapy on the serious risks and safe use, handling, and storage of LUMRYZ
- Evaluate patients within the first 3 months of starting LUMRYZ. It is recommended that patients be reevaluated every 3 months thereafter while taking LUMRYZ
- Report all potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Avadel CNS Pharmaceuticals, LLC

How Can Pharmacies Manage the Risk?

- Complete the *Patient Counseling Checklist* prior to dispensing LUMRYZ to new patients and existing patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer
- For patients who report a change in their medication use or medical history: Document and submit to the REMS using the *Patient Counseling Checklist*
- Notify prescribers when there are signs of potential abuse or misuse or when patients are taking sedative hypnotics, other CNS depressants, or other potentially interacting agents of which the prescriber is not already aware
- Report all potential adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, and death to Avadel CNS Pharmaceuticals, LLC
- Report any cases of suspected abuse, misuse, or diversion to the LUMRYZ REMS

TO ENROLL IN THE LUMRYZ REMS,
call 1-877-453-1029 or go to www.LUMRYZREMS.com.

Avadel

Reference ID: 5166429

Lumryz.
(sodium oxybate) for extended-release oral suspension C

WHAT ARE THE KEY REQUIREMENTS OF THE LUMRYZ REMS?

PRESCRIBERS

- Review the LUMRYZ Prescribing Information and *Prescriber Brochure*
- Complete and submit the *Prescriber Enrollment Form*
- Complete and submit the *Patient Enrollment Form* with each patient

PHARMACIES

- Ensure pharmacy staff and pharmacist training is complete and implement processes and procedures to comply with the LUMRYZ REMS
- Verify the prescriber is certified, the patient is enrolled, the patient has no other active, overlapping prescriptions for oxybate products, the patient and prescriber have not been disenrolled from other REMS for oxybate products for suspected abuse, misuse, or diversion, and obtain an authorization code prior to each dispense
- Complete and submit *Patient Counseling Checklist* prior to each dispense of LUMRYZ to counsel patients on therapy expectations, preparation and administration, precautions, and side effects of LUMRYZ for new patients, existing patients who are restarting LUMRYZ treatment after not receiving product for 6 months or longer, and patients who report a change in their medication use or medical history

PATIENTS

- Receive counseling from the prescriber on the serious risks associated with LUMRYZ and safe use, handling, and storage of LUMRYZ
- Enroll in the REMS by completing the *Patient Enrollment Form* with the prescriber
- Complete the *Patient Counseling Checklist* with the pharmacist

REPORTING ADVERSE EVENTS

Report adverse events to Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335 and/or to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This *Fact Sheet* does not contain the complete safety information for LUMRYZ. For complete safety information, please see the full Prescribing Information, including Boxed Warning, available at www.LUMRYZREMS.com.

MED-US-LUM-2100015
[REMS Approval Date]

**TO ENROLL IN THE LUMRYZ REMS,
call 1-877-453-1029 or go to www.LUMRYZREMS.com.**

Avadel

Reference ID: 5166429

Lumryz.
(sodium oxybate) for extended-release oral suspension C

INSTRUCTIONS

Risk Management Reports (RMRs) are completed by pharmacies that are certified in the LUMRYZ REMS to document and report events that give rise to a reasonable suspicion of abuse, misuse, diversion, or any behavior or information that may indicate LUMRYZ is not being used according to the prescriber's instructions. For immediate reporting, *RMRs* can be completed by the pharmacist online at www.LUMRYZREMS.com. Alternatively, a pharmacist can complete a print version and fax to the LUMRYZ REMS at 1-877-206-3198.

The *RMR* history allows for the review of prior events of suspected abuse, misuse, or diversion and gives the pharmacist a more complete picture of the patient's and/or prescriber's history. The availability of individual patient and prescriber *RMRs* enables the pharmacist to track and monitor for trends suggesting abuse, misuse, or diversion. A trend or pattern of behavior in a patient's and/or prescriber's *RMR* history can be an indicator of abuse, misuse, or diversion and identifies patients/prescribers who may require additional scrutiny when another event, such as an early refill request, occurs. In these cases, the *RMR* history informs actions of the pharmacist.

Examples of events that would require completion of an *RMR* under the LUMRYZ REMS include, but are not limited to, the following:

- Patient requests for early refills and/or prescriber approval of early refill requests.
- Patient's loss/misuse of the product.
- Patient claims he/she did not receive the product, but the delivery service shows receipt of delivery, or that the shipment was lost, stolen, or delivered to an incorrect address and was not returned.
- Tampering with, counterfeiting or contamination of the product.
- Inquiries and/or arrests by law and regulatory enforcement agencies associated with the misuse or diversion of the product, or crimes related to the product.

To complete an *RMR*:

- Complete investigation of the event, which may include contacting the patient, prescriber, law enforcement agency, or other parties.
- Complete review, follow-up, and sign the *RMR*.
  - When the event involves suspected abuse, misuse, or diversion, the prescriber will be contacted, as appropriate, and an alert may be placed in the prescriber database or patient database of the LUMRYZ REMS to ensure prescriber and pharmacist awareness.
  - The LUMRYZ REMS will monitor any associated patient or prescriber activity during the course of the investigation and for a period after the investigation, where appropriate.
  - The LUMRYZ REMS will work with Avadel CNS Pharmaceuticals, LLC to determine the need to notify local, state, or federal authorities.
- Attach any additional documentation required to support the investigation, including but not limited to the following: DEA Form 106, police or fire report, or report from the shipping service.
- Complete and submit the *RMR*, and any attachments, online at www.LUMRYZREMS.com or by fax to 1-877-206-3198 within one business day of awareness of the event.

If the *RMR* includes a potential adverse event, the potential adverse event is reported to Avadel CNS Pharmaceuticals, LLC at 1-888-828-2335 or productsafety@avadel.com.

ALL SECTIONS REQUIRED TO BE COMPLETED

REPORTER INFORMATION			
Type of Reporter (Select one): ☐ Patient ☐ Prescriber ☐ Pharmacist ☐ Other (specify):_____			
Name of Reporter, if not a patient:	First Name:	Last Name:	
PATIENT AND/OR PRESCRIBER ASSOCIATED WITH *RMR*			
☐ Patient	First Name:	Last Name:	Date of Birth (MM/DD/YYYY):
☐ Prescriber	First Name:	Last Name:	NPI No :

Lumryz.
(sodium oxybate) for extended-release oral suspension ℂ

ALL SECTIONS REQUIRED TO BE COMPLETED

LUMRYZ REMS RISK MANAGEMENT REPORT

Nature of Report:
☐ Early Refill Request ☐ Lost/Stolen Product ☐ Package Not Received ☐ Abuse ☐ Misuse
☐ Diversion ☐ Product tampering by an individual in contact with product ☐ Counterfeit/contaminated product
☐ Unexplained irreconcilable inventory ☐ Prescriber's DEA and/or state license is invalid
☐ Suicide attempt and/or ideation and/or death ☐ Multiple prescribers ☐ Potential or actual dose increase
☐ Excess medication on hand

If early refill request, what is the reason? ☐ Dose Increase ☐ Spilled Medication ☐ Lost/Stolen Product
☐ Other (specify):_____

Have the alerts and *RMR* history been reviewed for the patient? ☐ Yes ☐ No | Date(s) of RMR Event:

RMR Event (please provide detail):

Potential adverse event (AE) associated with report? ☐ Yes ☐ No
If yes, date AE reported to Avadel CNS Pharmaceuticals, LLC:_____
If yes, AE report number (if available):_____

Prescriber Contacted? ☐ Yes ☐ No
If yes, what was the outcome? ☐ Early Refill Approved ☐ Early Refill Denied
☐ Recommend to Disenroll Patient ☐ Other (specify):_____
If no, what is the reason? ☐ Unable to Contact ☐ Other (specify):_____

Summary of investigation:

Attachments, if applicable: ☐ DEA Form 106 ☐ Police/Fire Report ☐ Shipping Service Report ☐ Other (specify):_____
Total number of additional pages: _____

Should patient be monitored (alert placed)? ☐ Yes ☐ No

Are you requesting disenrollment for suspected abuse, misuse, or diversion? ☐ Yes ☐ No
If yes, for whom? ☐ Patient ☐ Prescriber

PHARMACY INFORMATION

Pharmacy Name:	NPI No :
Pharmacist in Charge First Name:	Pharmacist in Charge Last Name:

_____ Signature _____ Date

Report adverse events to Avadel CNS Pharmaceuticals, LLC at 1-888-828-2335 or productsafety@avadel.com.

Avadel

Placeholder for LUMRYZ REMS Overview Video

LUMRYZ™ REMS (Risk Evaluation and Mitigation Strategy)

The LUMRYZ REMS (Risk Evaluation and Mitigation Strategy) is a safety program that manages the risks of serious adverse outcomes resulting from inappropriate prescribing, misuse, abuse, and diversion of LUMRYZ. The LUMRYZ REMS is required by the Food and Drug Administration (FDA) to ensure the potential benefits of LUMRYZ outweigh its risks.

Prescribers

Prescribers must become certified in the LUMRYZ REMS to prescribe LUMRYZ.

Learn about Prescriber Certification

LEARN MORE

Patients

Patients who are prescribed LUMRYZ must be enrolled in the LUMRYZ REMS.

Learn about Patient Enrollment

LEARN MORE

If you have questions about the LUMRYZ REMS or need help with certification or enrollment, call 1-877-453-1029
Monday-Friday,
8:00 AM – 8:00 PM ET

To learn more about the serious risks associated with LUMRYZ, please refer to the Prescribing Information including Boxed Warning and the Medication Guide.

INDICATION

LUMRYZ is a central nervous system depressant indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.

Prescribers

LUMRYZ is only available through the LUMRYZ REMS. In order for prescribers to prescribe LUMRYZ, they must become certified.

To become certified in the LUMRYZ REMS, prescribers must:

1. Review the LUMRYZ Prescribing Information and the *Prescriber Brochure*
2. Complete, sign and submit a *Prescriber Enrollment Form* to the LUMRYZ REMS:
   - Online
   - By fax to 1-877-206-3198

To enroll a patient in the LUMRYZ REMS:

1. Complete the *Patient Enrollment Form* with each patient and submit it to the LUMRYZ REMS:
   - Online
   - By fax to 1-877-206-3198

Administration Requirements:

Before treatment initiation, the prescriber will:

1. Assess the patient's health status to determine if LUMRYZ is medically appropriate by screening for:
   - History of alcohol and drug abuse, sleep-related breathing disorders, compromised respiratory function, depression and suicidality
   - Concomitant use of sedative hypnotics, other CNS depressants or other potentially interacting agents
2. Counsel the patient on:
   - The serious risks and safe use, handling and storage of LUMRYZ using the *Patient Brochure*
3. Submit a *Prescription Form* to a certified pharmacy

During treatment, within the first 3 months of starting treatment and recommended every 3 months thereafter, the prescriber will:

1. Assess the patient for concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents, serious adverse events, and signs of abuse and misuse, including an increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, and/or drug-seeking behavior

At all times, the prescriber will:

1. Report all potential serious adverse events including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335.
2. Report requests to disenroll a patient to a certified pharmacy.

LUMRYZ™ REMS Prescriber Enrollment Form

Complete and submit this form online at www.LUMRYZREMS.com,
OR fax to 1-877-206-3198 (toll free).
For more information, please call the LUMRYZ REMS at 1-877-453-1029.

TO BECOME A CERTIFIED PRESCRIBER IN THE LUMRYZ REMS AND PRESCRIBE LUMRYZ:

1. Review the LUMRYZ Prescribing Information.
2. Review the *Prescriber Brochure*.
3. Complete steps 1, 2 and 3 below and submit this *Prescriber Enrollment Form* to the LUMRYZ REMS.

STEP 1 PRESCRIBER ATTESTATIONS

I have:

- Reviewed the Prescribing Information.
- Reviewed the *Prescriber Brochure*.

I understand:

- LUMRYZ is approved for the treatment of
  - Cataplexy in adults with narcolepsy.
  - Excessive daytime sleepiness (EDS) in adults with narcolepsy.
- LUMRYZ is a Schedule III central nervous system (CNS) depressant and can cause obtundation and clinically significant respiratory depression at recommended doses.
- LUMRYZ is contraindicated in combination with alcohol and sedative hypnotics.
- Concurrent use of LUMRYZ with certain other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptic drugs, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death.
- Patients who have sleep apnea or compromised respiratory function (e.g., asthma, COPD, etc.) may be at higher risk of developing respiratory depression, loss of consciousness, coma, and death with LUMRYZ use.

Before treatment initiation (first dose), I must:

- Screen for history of alcohol and drug abuse, sleep-related breathing disorders, compromised respiratory function, depression, suicidality, concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents. Document my findings on the *Prescription Form*.
- Counsel the patient on the serious risks and safe use, handling, and storage of LUMRYZ using the *Patient Brochure*.
- Enroll the patient by completing and submitting the *Patient Enrollment Form* to the REMS.
- Order LUMRYZ using the *Prescription Form* and submit it to a certified pharmacy.

Before treatment re-initiation, I must:

- **For patients disenrolled for suspicion of abuse, misuse, or diversion**: Communicate with the pharmacy regarding all relevant patient history and re-enroll the patient if the pharmacist and I agree.
- **For patients with a lapse in treatment of 6 months or longer**: Order LUMRYZ using the *Prescription Form* and submit it to a certified pharmacy.

Within the first 3 months of starting treatment, I must:

- Assess the patient for concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents, serious adverse events, and signs of abuse and misuse, including an increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, and/or drug-seeking behavior.

It is recommended that patients be re-assessed every 3 months while taking LUMRYZ.

I must:

- Report potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Avadel CNS Pharmaceuticals, LLC.
- Report requests to disenroll a patient to a certified pharmacy.

STEP 2 TO HELP EXPEDITE THE ENROLLMENT PROCESS, PLEASE COMPLETE ALL REQUIRED FIELDS

Prescriber Information (* *denotes required field*)

*NPI No.

CONTINUE

LUMRYZ™ REMS Prescriber Enrollment Form

Complete and submit this form online at www.LUMRYZREMS.com,
OR fax to 1-877-206-3198 (toll free).
For more information, please call the LUMRYZ REMS at 1-877-453-1029.

TO BECOME A CERTIFIED PRESCRIBER IN THE LUMRYZ REMS AND PRESCRIBE LUMRYZ:

1. Review the LUMRYZ Prescribing Information.
2. Review the *Prescriber Brochure*.
3. Complete steps 1, 2 and 3 below and submit this *Prescriber Enrollment Form* to the LUMRYZ REMS.

STEP 1 PRESCRIBER ATTESTATIONS

I have:
- Reviewed the Prescribing Information.
- Reviewed the *Prescriber Brochure*.

I understand:
- LUMRYZ is approved for the treatment of
  - Cataplexy in adults with narcolepsy.
  - Excessive daytime sleepiness (EDS) in adults with narcolepsy.
- LUMRYZ is a Schedule III central nervous system (CNS) depressant and can cause obtundation and clinically significant respiratory depression at recommended doses.
- LUMRYZ is contraindicated in combination with alcohol and sedative hypnotics.
- Concurrent use of LUMRYZ with certain other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptic drugs, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death.
- Patients who have sleep apnea or compromised respiratory function (e.g., asthma, COPD, etc.) may be at higher risk of developing respiratory depression, loss of consciousness, coma, and death with LUMRYZ use.

Before treatment initiation (first dose), I must:
- Screen for history of alcohol and drug abuse, sleep-related breathing disorders, compromised respiratory function, depression, suicidality, concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents. Document my findings on the *Prescription Form*.
- Counsel the patient on the serious risks and safe use, handling, and storage of LUMRYZ using the *Patient Brochure*.
- Enroll the patient by completing and submitting the *Patient Enrollment Form* to the REMS.
- Order LUMRYZ using the *Prescription Form* and submit it to a certified pharmacy.

Before treatment re-initiation, I must:
- **For patients disenrolled for suspicion of abuse, misuse, or diversion**: Communicate with the pharmacy regarding all relevant patient history and re-enroll the patient if the pharmacist and I agree.
- **For patients with a lapse in treatment of 6 months or longer**: Order LUMRYZ using the *Prescription Form* and submit it to a certified pharmacy.

Within the first 3 months of starting treatment, I must:
- Assess the patient for concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents, serious adverse events, and signs of abuse and misuse, including an increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, and/or drug-seeking behavior.

It is recommended that patients be re-assessed every 3 months while taking LUMRYZ.

I must:
- Report potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Avadel CNS Pharmaceuticals, LLC.
- Report requests to disenroll a patient to a certified pharmacy.

STEP 2 TO HELP EXPEDITE THE ENROLLMENT PROCESS, PLEASE COMPLETE ALL REQUIRED FIELDS

Prescriber Information (* *denotes required field*)

*NPI No.
1234567890

*First Name: John | M.I. | *Last Name: Smith | *DEA No.

Facility/Practice Name | *State License No.

*Professional Designation
☐ MD ☐ DO ☐ PA ☐ NP ☐ Other

*Medical Specialty
☐ Sleep Medicine ☐ Neurology ☐ Pulmonology ☐ Psychiatry ☐ Internal Medicine ☐ Other

*Address Line 1: 123 Main Street | Address Line 2

*City: Philadelphia | *State: PA | *Zip Code: 99999

*Phone | *Fax | *Email

*Preferred Method of Contact
☐ Email ☐ Fax

Office Contact First Name | Office Contact Last Name | Office Contact Phone

STEP 3 PRESCRIBER SIGNATURE IS REQUIRED BELOW FOR ENROLLMENT IN THE LUMRYZ REMS

By signing below, I acknowledge the above attestations, and I understand my personally identifiable information provided above will be shared with Avadel CNS Pharmaceuticals, LLC, its agents, contractors, and affiliates and entered into a prescriber database for the LUMRYZ REMS. I agree that I may be contacted in the future by mail, email, fax, and/or telephone concerning LUMRYZ, the LUMRYZ REMS, and other LUMRYZ programs and services.

☐ *Prescriber Signature

CANCEL | SUBMIT

Report adverse events to Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335.

LUMRYZ™ REMS Prescriber Enrollment Form

Complete and submit this form online at www.LUMRYZREMS.com,
OR fax to 1-877-206-3198 (toll free).
For more information, please call the LUMRYZ REMS at 1-877-453-1029.

TO BECOME A CERTIFIED PRESCRIBER IN THE LUMRYZ REMS AND PRESCRIBE LUMRYZ:

1. Review the LUMRYZ Prescribing Information.
2. Review the *Prescriber Brochure*.
3. Complete steps 1, 2 and 3 below and submit this *Prescriber Enrollment Form* to the LUMRYZ REMS.

STEP 1 PRESCRIBER ATTESTATIONS

I have:
- Reviewed the Prescribing Information.
- Reviewed the *Prescriber Brochure*.

I understand:
- LUMRYZ is approved for the treatment of
  - Cataplexy in adults with narcolepsy.
  - Excessive daytime sleepiness (EDS) in adults with narcolepsy.
- LUMRYZ is a Schedule III central nervous system (CNS) depressant and can cause obtundation and clinically significant respiratory depression at recommended doses.
- LUMRYZ is contraindicated in combination with alcohol and sedative hypnotics.
- Concurrent use of LUMRYZ with certain other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptic drugs, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death.
- Patients who have sleep apnea or compromised respiratory function (e.g., asthma, COPD, etc.) may be at higher risk of developing respiratory depression, loss of consciousness, coma, and death with LUMRYZ use.

Before treatment initiation (first dose), I must:
- Screen for history of alcohol and drug abuse, sleep-related breathing disorders, compromised respiratory function, depression, suicidality, concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents. Document my findings on the *Prescription Form*.
- Counsel the patient on the serious risks and safe use, handling, and storage of LUMRYZ using the *Patient Brochure*.
- Enroll the patient by completing and submitting the *Patient Enrollment Form* to the REMS.
- Order LUMRYZ using the *Prescription Form* and submit it to a certified pharmacy.

Before treatment re-initiation, I must:
- **For patients disenrolled for suspicion of abuse, misuse, or diversion**: Communicate with the pharmacy regarding all relevant patient history and re-enroll the patient if the pharmacist and I agree.
- **For patients with a lapse in treatment of 6 months or longer**: Order LUMRYZ using the *Prescription Form* and submit it to a certified pharmacy.

Within the first 3 months of starting treatment, I must:
- Assess the patient for concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents, serious adverse events, and signs of abuse and misuse, including an increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, and/or drug-seeking behavior.

It is recommended that patients be re-assessed every 3 months while taking LUMRYZ.

I must:
- Report potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Avadel CNS Pharmaceuticals, LLC.
- Report requests to disenroll a patient to a certified pharmacy.

STEP 2 TO HELP EXPEDITE THE ENROLLMENT PROCESS, PLEASE COMPLETE ALL REQUIRED FIELDS

Prescriber Information (* *denotes required field*)

*NPI No.
1234567890

*First Name: John
M.I.:
*Last Name: Smith
*DEA No.:

Facility/Practice Name:
*State License No.:

*Professional Designation
☐ MD ☐ DO ☐ PA ☐ NP ☑ Other

*Medical Specialty
☐ Sleep Medicine ☐ Neurology ☐ Pulmonology ☐ Psychiatry ☐ Internal Medicine ☑ Other

*Professional Designation Other: RN
*Medical Specialty Other: Internist

*Address Line 1: 123 Main Street
Address Line 2:

*City: Philadelphia
*State: PA
*Zip Code: 99999

*Phone:
*Fax:
*Email:

*Preferred Method of Contact
☐ Email ☐ Fax

Office Contact First Name:
Office Contact Last Name:
Office Contact Phone:

STEP 3 PRESCRIBER SIGNATURE IS REQUIRED BELOW FOR ENROLLMENT IN THE LUMRYZ REMS

By signing below, I acknowledge the above attestations, and I understand my personally identifiable information provided above will be shared with Avadel CNS Pharmaceuticals, LLC, its agents, contractors, and affiliates and entered into a prescriber database for the LUMRYZ REMS. I agree that I may be contacted in the future by mail, email, fax, and/or telephone concerning LUMRYZ, the LUMRYZ REMS, and other LUMRYZ programs and services.

☐ *Prescriber Signature

CANCEL SUBMIT

Report adverse events to Avadel CNS Pharmaceuticals, LLC at productsafety@avadel.com or 1-888-828-2335.

LUMRYZ REMS Prescriber Enrollment Successful

You have successfully completed and submitted the *Prescriber Enrollment Form*. A confirmation of this submission has been sent via your preferred method of contact.

You can expect to receive an email containing a link to login and instructions for creating a password. Please login with the username provided. You will then be prompted to create a password.

If you do not receive the email within the next few hours, or would like to update your enrollment information at any time, please contact the LUMRYZ REMS for assistance at 1-877-453-1029.

Patients

LUMRYZ is available only through the LUMRYZ REMS. For a patient to receive LUMRYZ, the prescriber must enroll the patient in the LUMRYZ REMS.

To become enrolled in the LUMRYZ REMS, patients must:

1. Discuss the benefits, risks and safe use of LUMRYZ with your prescriber
2. Ask your prescriber any questions you have about taking LUMRYZ and about the LUMRYZ REMS
3. Make sure you understand:
   - How to enroll and take part in the LUMRYZ REMS
   - The information in the *Patient Brochure*
   - The benefits and serious risks associated with LUMRYZ
   - The safe use, handling and storage of LUMRYZ
4. Together with your doctor, complete and sign the *Patient Enrollment Form*
   - *Patient Enrollment Form*
5. Complete the *Patient Counseling Checklist* with the pharmacist based on changes in your medication and/or medical history
6. Your healthcare provider will evaluate you within the first 3 months of taking LUMRYZ and may reevaluate you every 3 months while you are taking LUMRYZ
   - Inform your prescriber and the pharmacy about any changes in your medications or medical conditions

Resources

Resources for Prescribers

- *Prescriber Brochure*
- *Fact Sheet*
- *Prescriber Enrollment Form*
- *Patient Enrollment Form*
- *Prescription Form*
- *Dear Healthcare Provider Letter*
- *Dear Professional Society Letter*

Resources for Pharmacies

- *Certified Pharmacy Training Program*
- *Patient Counseling Checklist*

Resources for Patients

- *Patient Brochure*
- Medication Guide
- *Patient Enrollment Form*

Contact Us

Phone: 1-877-453-1029

Fax: 1-877-206-3198

Hours of Operation: Monday - Friday
8:00 AM — 8:00 PM Eastern Time

To learn more about the serious risks associated with LUMRYZ, please refer to the Prescribing Information including Boxed Warning and the Medication Guide.

Pharmacy Staff Registration

Please contact your pharmacy's authorized representative for the LUMRYZ REMS if you do not know your Pharmacy Identifier.

Required fields are denoted by "*".

Pharmacy Staff User Information

* Pharmacy Identifier

CANCEL CONTINUE

Pharmacy Staff Registration

Please contact your pharmacy's authorized representative for the LUMRYZ REMS if you do not know your Pharmacy Identifier.

Required fields are denoted by "*".

Pharmacy Staff User Information

* Pharmacy Identifier

1111

You are registering for the below pharmacy. If this pharmacy is incorrect, please check the Pharmacy Identifier and if in error, click "Clear".

ABC Pharmacy

* I am a Pharmacist

○ Yes ○ No

* First Name

* Last Name

* Email Address

* Phone

CLEAR SUBMIT

Pharmacy Staff Registration

Your registration has been successfully submitted.

You can expect to receive an email containing a link to login and instructions for creating a password. Please login with the username provided. You will then be prompted to create a password.

If you do not receive the email within the next few hours, or would like to update your information at any time, please contact the LUMRYZ REMS for assistance at 1-877-453-1029.

Lumryz

(sodium oxybate) for extended-release oral suspension Ⓒ

Login is available to certified prescribers to enroll patients, and to certified pharmacy users to complete and submit *Knowledge Assessments, Risk Management Reports* and *Patient Counseling Checklists*.

Certified pharmacies are also able to verify patient REMS requirements are met prior to dispensing LUMRYZ.