# Risk Evaluation and Mitigation Strategies: From Burden to Benefit

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## INTRODUCTION

- Risk Evaluation and Mitigation Strategies (REMS) are safety programs required by the US Food and Drug Administration (FDA) for certain medications to ensure the benefits of the medication outweigh the risks[1]
  - REMS are not designed to mitigate all medication-related adverse events, as these are outlined in the prescribing information, but instead target specific serious risks through measures designed to prevent, monitor, or reduce their impact
- REMS with Elements to Ensure Safe Use (ETASU) are a class-wide requirement for oxybate medications, which include extended-release sodium oxybate (SXB; LUMRYZ®; Avadel Pharmaceuticals, Chesterfield, MO), immediate-release SXB, and immediate-release calcium, magnesium, potassium, and sodium (mixed-salt) oxybates[2-5]
  - REMS are required for oxybates because they contain a sodium salt of gamma-hydroxybutyrate, a central nervous system depressant with a known risk for abuse and misuse[2-5]
- Oxybate REMS are important programs that ensure safe and appropriate use and prescribing, facilitate secure handling to prevent diversion or unintended exposure, and provide infrastructure for documentation and communication of concerning behaviors[6]
- For providers and patients unaccustomed to REMS with ETASU programs, the oxybate REMS process may be perceived as daunting, which may may pose a barrier to patient access to an important treatment option[7]

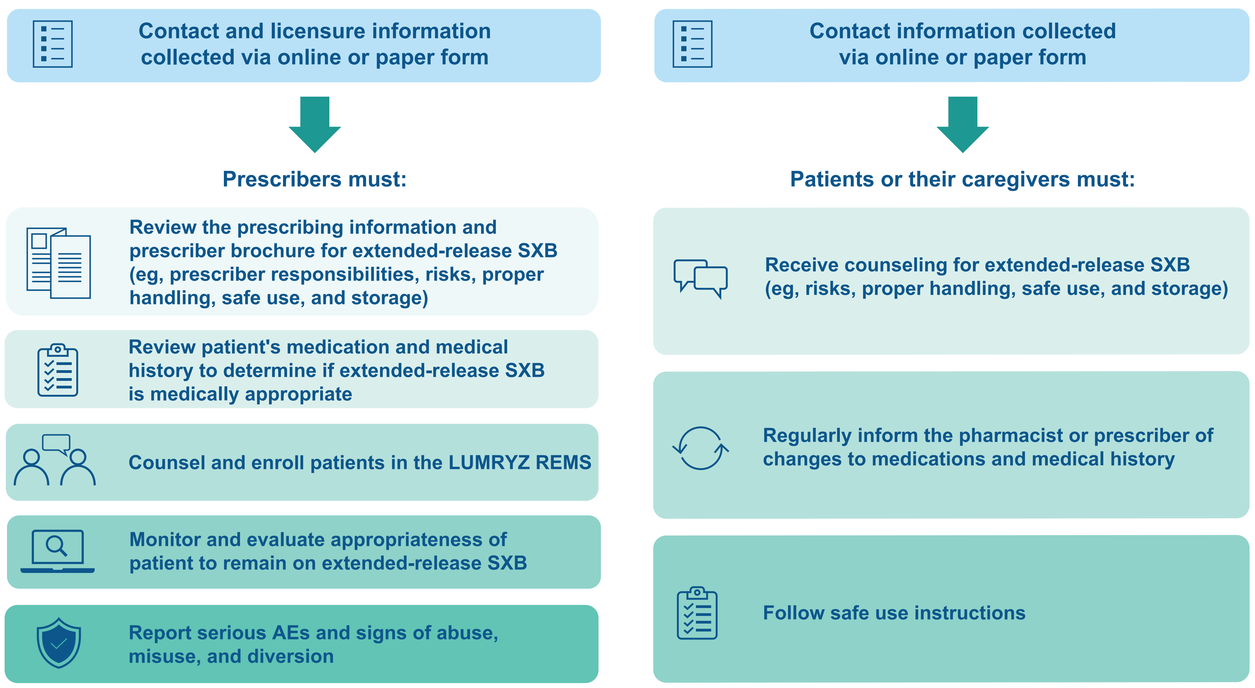
## OBJECTIVE

- To describe the process and tasks for prescriber and pharmacy enrollment and certification, patient enrollment, and ongoing activities to ensure safe and appropriate use of extended-release SXB in the LUMRYZ REMS

## LUMRYZ REMS PROCESS

- Prescribers and patients may enroll in the LUMRYZ REMS via an online or single-page paper form, with prescribers becoming certified after their Drug Enforcement Administration (DEA), National Provider Identifier (NPI), and state licenses are verified and they attest to having reviewed the extended-release SXB prescribing information and prescriber brochure (**Figure 1**)
  - Online enrollment enables same-day prescriber certification
  - The office-contact portal allows for online initiation of patient enrollment and management of tasks and communication

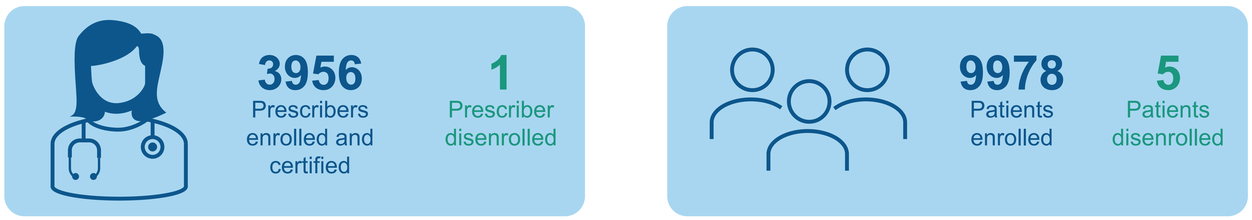
### FIGURE 1: Prescriber and Patient Enrollment in LUMRYZ REMS




AE, adverse event; SXB, sodium oxybate.

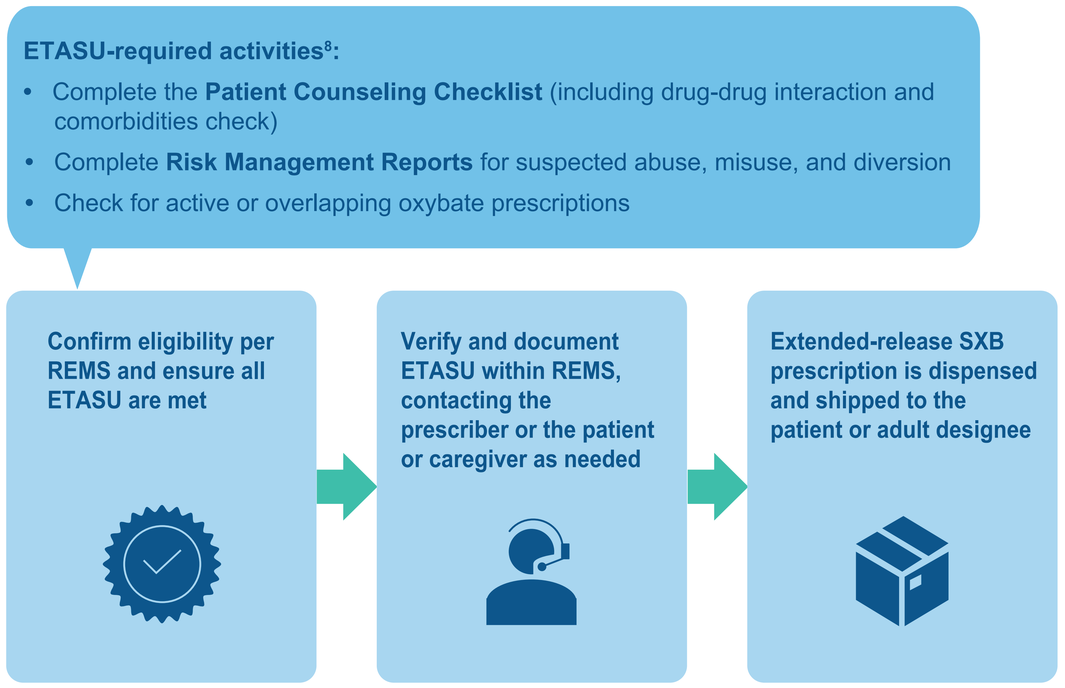
- Between May 1, 2023 (start date) and April 30, 2026, nearly 4000 prescribers were enrolled and certified and nearly 10,000 patients were enrolled in LUMRYZ REMS (**Figure 2**)
  - Only 1 prescriber and 5 patients were disenrolled from LUMRYZ REMS due to suspected abuse, misuse, or diversion

### FIGURE 2: Current Prescriber Certification and Patient Enrollment




- Prior to dispensing and shipping every initial prescription and refill, pharmacists at 4 LUMRYZ REMS–certified pharmacies confirm that patients are eligible for oxybate treatment by verifying and documenting within the REMS that all ETASU are met (**Figure 3**)

### FIGURE 3: Certified Pharmacy Processes for LUMRYZ REMS




ETASU, Elements to Assure Safe Use; REMS, Risk Evaluation and Mitigation Strategies; SXB, sodium oxybate.

- The manufacturer continuously monitors for noncompliance, intermittently assesses stakeholder understanding, and conducts cumulative analyses to confirm the REMS is operating as required to protect patients and prescribers (**Figure 4**)

### FIGURE 4: Manufacturer Oversight of LUMRYZ REMS


FDA, US Food and Drug Administration; REMS, Risk Evaluation and Mitigation Strategies.

## CONCLUSIONS

- REMS are important programs that help to ensure patient safety
- Greater understanding of REMS requirements for oxybates, communication with REMS-certified pharmacists, and education of patients about the REMS are essential to reduce perceived barriers to access and to support safe, compliant oxybate use

## ACKNOWLEDGMENTS

Medical writing support was provided by Taylor Johnson, PharmD, from Citrus Health Group, Inc. (Chicago, IL) and was funded by Avadel Pharmaceuticals (Chesterfield, MO).

## FUNDING

This work was funded by Avadel Pharmaceuticals (Chesterfield, MO). *Avadel Pharmaceuticals Limited (formerly Avadel Pharmaceuticals plc) is an affiliate of Alkermes plc. LUMRYZ® is a registered trademark of Flamel Ireland Limited, an affiliate of Alkermes plc.

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## DISCLOSURES

**LMM** served on a narcolepsy advisory board of Jazz Pharmaceuticals.

**CC** has served on the advisory board of AbbVie, Acadia, Alkermes, Inc., Axsome Therapeutics, Biogen, Bristol Myers Squibb, Corium, Lilly, Idorsia, Intra-Cellular, Jazz Pharmaceuticals, Johnson & Johnson, Lundbeck, Moderna, Neurocrine, Otsuka, Sage Therapeutics, Sumitomo Pharma, and Teva Pharmaceuticals; his spouse has served on an advisory board for Bristol Myers Squibb and Otsuka; has been a consultant for AbbVie, Acadia, Alkermes, Inc., Axsome Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Corium, Lilly, Intra-Cellular, Johnson & Johnson, Lundbeck, MedinCell, Moderna, Neurocrine, Otsuka, Sage Therapeutics, Sumitomo Pharma, Supernus, and Teva Pharmaceuticals; has received research grants from Acadia, Axsome Therapeutics, Harmony Biosciences, Neurocrine, and Teva Pharmaceuticals; has received speaker/promotional honoraria from AbbVie, Acadia, Alkermes, Inc., Axsome Therapeutics, Bristol Myers Squibb, Corium, Intra-Cellular, Johnson & Johnson, Lundbeck, Luye, Merck, Neurocrine, Otsuka, Sumitomo Pharma, and Teva Pharmaceuticals; and has no stocks/stock options/ownership interest/patents.

**RKB** is a shareholder in Watermark Medical and Healthy Humming, LLC; serves on the board of directors for Watermark Medical; is a consultant for Jazz Pharmaceuticals, Takeda Pharmaceutical Co., and Oventus; has received industry funding for research from Avadel Pharmaceuticals, BresoTec, Bayer, Idorsia, Suven Life Sciences Ltd., Jazz Pharmaceuticals, Balance Therapeutics, Vanda Pharmaceuticals, Merck & Co., Eisai, Philips, FRESCA Medical, Takeda Pharmaceutical Co., LivaNova, Roche, and Sommetrics; and has served on speakers bureaus for Jazz Pharmaceuticals, Eisai, and Harmony Biosciences.

**MC** has served as a speaker for Avadel Pharmaceuticals and Axsome Therapeutics and as a consultant for Jazz Pharmaceuticals.

**DA**, **MS,** and **DB** are employees of Alkermes, Inc.

**JG** was an employee of Avadel Pharmaceuticals and is a consultant to Alkermes, Inc.

**TG** is an employee of United BioSource, LLC (UBC).