

Sodium Oxybate REMS
Program Prescriber Brochure

Dear Prescriber,

Welcome to the Sodium Oxybate REMS Program, which 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 that the benefits of the drug outweigh its risks.

This brochure provides valuable information about the Sodium Oxybate REMS Program that includes important prescribing information, educational and counseling requirements, and materials necessary for program certification and prescribing sodium oxybate oral solution, including:

- *Sodium Oxybate REMS Program Prescriber Enrollment Form* – a one-time certification is required for all prescribers of sodium oxybate.
- *Sodium Oxybate REMS Program Patient Enrollment Form* – a one-time patient enrollment in the Sodium Oxybate REMS Program is required for each new patient for whom sodium oxybate will be prescribed.
- *Sodium Oxybate REMS Program Prescription Form* – required for prescribing sodium oxybate. This form must be used for new prescriptions and may also be used for refills and renewals of sodium oxybate prescriptions.
- *Sodium Oxybate REMS Program Patient Quick Start Guide* – answers important questions for patients about how to get sodium oxybate, how to use sodium oxybate properly, and how to store it safely. It also gives important information about the risks associated with sodium oxybate.

The *Sodium Oxybate REMS Program Prescriber Enrollment Form* and *Sodium Oxybate REMS Program Patient Enrollment Form* must be completed in full and sent to the Sodium Oxybate REMS Program. The *Sodium Oxybate REMS Program Prescription Form* must be completed in full and sent to one of the certified pharmacies. For your convenience, the *Sodium Oxybate REMS Program Prescriber Enrollment Form* and the *Sodium Oxybate REMS Program Patient Enrollment Form* are available online at www.SodiumOxybateREMSProgram.com and all three forms can be requested by calling the Sodium Oxybate REMS Program toll-free at 855-705-2424. A certified pharmacy in the Sodium Oxybate REMS Program is responsible for processing prescriptions for sodium oxybate.

Continue reading this brochure to learn more about the Sodium Oxybate REMS Program and your responsibilities as a prescriber of sodium oxybate. Please review the Prescribing Information (PI) for sodium oxybate.

Sodium oxybate may be dispensed only to patients enrolled in the Sodium Oxybate REMS Program.

Sodium oxybate is approved for:

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

If you require any additional assistance or information, please call the Sodium Oxybate REMS Program at 855-705-2424 or visit www.SodiumOxybateREMSProgram.com.

Sincerely,

Sodium Oxybate sponsors

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- Sodium oxybate is contraindicated in patients being treated with sedative hypnotics.
- Patients should not drink alcohol when using sodium oxybate.
- Sodium oxybate is contraindicated in patients with succinic semialdehyde dehydrogenase deficiency.

WARNINGS AND PRECAUTIONS

CNS Depression

- Sodium oxybate is a CNS depressant. Concurrent use of sodium oxybate with other CNS depressants, including but not limited to opioid analgesics; benzodiazepines; sedating antidepressants, antipsychotics, or anti-epileptics; 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 sodium oxybate is required, dose reduction or discontinuation of one or more CNS depressants (including sodium oxybate) should be considered.
 - If short-term use of an opioid (e.g., post- or perioperative) is required, interruption of treatment with sodium oxybate 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 sodium oxybate use.

Healthcare providers should caution patients about operating hazardous machinery for the first 6 hours after taking a dose of sodium oxybate.

Abuse and Misuse

- Sodium oxybate is a Schedule III controlled substance.
- 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 events, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death. Illicit GHB has also been associated with drug-facilitated sexual assault.
- The rapid onset of sedation, coupled with the amnesic features of sodium oxybate, 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 sodium oxybate (e.g. increase in size or frequency of dosing; reports of lost, stolen, or spilled medication; drug-seeking behavior; feigned cataplexy).

Sodium Oxybate REMS Program

- Sodium oxybate is to be prescribed only to patients enrolled in the Sodium Oxybate REMS Program. Sodium oxybate is available only through a restricted distribution program called the Sodium Oxybate REMS Program. Required components of the Sodium Oxybate REMS Program are:
 - Healthcare providers who prescribe sodium oxybate must be certified. To be certified, prescribers must complete the *Sodium Oxybate REMS Program Prescriber Enrollment Form* and comply with the Sodium Oxybate REMS Program requirements.
 - Sodium oxybate will be dispensed only by pharmacies that are certified.
 - Sodium oxybate will be shipped only to enrolled patients with documentation of safe use conditions. To be enrolled, patients must sign the *Sodium Oxybate REMS Program Patient Enrollment Form* and acknowledge that they have been counseled on the serious risks and safe use of sodium oxybate.

Further information is available at www.SodiumOxybateREMSProgram.com or 855-705-2424.

Depression, Suicidality, and Other Behavioral/Neuropsychiatric Adverse Events

- The emergence of depression in patients treated with sodium oxybate was seen in clinical trials and requires careful and immediate attention. Patients with a previous history of a depressive illness and/or suicide attempt should be monitored especially carefully for the emergence of depressive symptoms while taking sodium oxybate. Sodium oxybate can cause the emergence of neuropsychiatric adverse events (psychosis, paranoia, hallucination, and agitation), loss of consciousness, and sleepwalking. Patients should be instructed to call their healthcare provider if they experience any of these events.
- Anxiety can also occur in patients treated with sodium oxybate.

Use in Patients Sensitive to High Sodium Intake

- Sodium oxybate has a high sodium content.
- Daily sodium intake should be considered in patients on salt-restricted diets or with heart failure, hypertension, or compromised renal function.

Most Common Adverse Events

- In three controlled clinical trials, the most common adverse reactions (incidence 25% and twice the rate seen with placebo) in sodium oxybate -treated patients were nausea (20%), dizziness (15%), vomiting (11%), somnolence (8%), enuresis (7%), and tremor (5%).
- Of the 398 sodium oxybate treated patients with narcolepsy, 10.3% of patients discontinued because of adverse reactions compared with 2.8% of patients receiving placebo. The most common adverse reaction leading to discontinuation was nausea (2.8%). The majority of adverse reactions leading to discontinuation began during the first few weeks of treatment.
- Please see PI for sodium oxybate.

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Prescribing Information and a Medication Guide are also included.

PRESCRIBING SODIUM OXYBATE – A BRIEF GUIDE

The procedure for writing and dispensing prescriptions for sodium oxybate is outlined below.

PRESCRIBERS OF SODIUM OXYBATE

Prescribing sodium oxybate requires a one-time certification.

- If you are prescribing sodium oxybate for the first time, complete the *Sodium Oxybate REMS Program Prescriber Enrollment Form*, found either in this *Sodium Oxybate REMS Program Prescriber Brochure* or online at www.SodiumOxybateREMSProgram.com. If you choose not to complete the *Sodium Oxybate REMS Program Prescriber Enrollment Form* online, please fax it to the Sodium Oxybate REMS Program at 800-353-0987 or mail to Sodium Oxybate REMS Program, PO Box XXXXX, City, ST XXXXX-XXXX.
- On the *Sodium Oxybate REMS Program Prescriber Enrollment Form*, please confirm that:
 - You understand that sodium oxybate is approved for:
 - Treatment of cataplexy in patients with narcolepsy
 - Treatment of excessive daytime sleepiness (EDS) in patients with narcolepsy
 - You have read and understand the PI and this *Sodium Oxybate REMS Program Prescriber Brochure*
 - You agree to screen each 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
 - You agree to counsel your patients on:
 - The serious risks associated with sodium oxybate
 - Contraindications (alcohol and sedative hypnotics)
 - Risks of concomitant use of sodium oxybate with alcohol and/or other CNS depressants
 - Risk of operating hazardous machinery, including automobiles or airplanes, for the first 6 hours after taking a dose of sodium oxybate
 - Preparation and dosing instructions for sodium oxybate
 - Risk of abuse and misuse associated with use of sodium oxybate
 - Safe use, handling, and storage of sodium oxybate
 - You will enroll each patient in the Sodium Oxybate REMS Program by completing the one-time *Sodium Oxybate REMS Program Patient Enrollment Form* and submitting the form to the Sodium Oxybate REMS Program
 - You will evaluate each patient within the first 3 months of starting sodium oxybate, including an evaluation of the following. It is recommended that patients be re-evaluated every 3 months thereafter while on sodium oxybate therapy:
 - Patient's concomitant medications
 - Serious adverse events
 - Signs of abuse and misuse such as an increase in dose or frequency of dosing; reports of lost, stolen, or spilled medication; and/or drug seeking behavior
 - You will report all potential serious adverse events including CNS depression, respiratory depression, loss of consciousness, coma, and death, and any cases of suspected abuse, misuse, or diversion to the Sodium Oxybate REMS Program

PRESCRIBING SODIUM OXYBATE A BRIEF GUIDE (CONT'D)

- On the *Sodium Oxybate REMS Program Patient Enrollment Form*:
 - Verify that you have provided counseling to each patient about the serious risks associated with the use of sodium oxybate and the safe use conditions as described in the *Sodium Oxybate REMS Program Patient Quick Start Guide*
 - Obtain mandatory patient signature acknowledging that he/she has been counseled on the serious risks and safe use conditions of sodium oxybate and has had the opportunity to ask you any questions he/she may have about sodium oxybate, and the patient grants you the authority to release personal information to the Sodium Oxybate REMS Program, other Sodium Oxybate REMS Programs and its business partners and agents, including the certified pharmacy that will fill the prescription
 - Fax the completed *Sodium Oxybate REMS Program Patient Enrollment Form* to the Sodium Oxybate REMS Program at 855-705-2424, complete online at www.SodiumOxybateREMSProgram.com, or mail to Sodium Oxybate REMS Program, PO Box XXXXX, City, ST XXXXX-XXXX

PRESCRIBING REQUIREMENTS

- Write prescriptions for both new and existing patients using the *Sodium Oxybate REMS Program Prescription Form*. If the patient has a lapse in therapy for 6 months or more, a new prescription will be required.
 - Fill out the 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 sodium oxybate
 - Contraindications (alcohol and sedative hypnotics)
 - The risks of concomitant use of alcohol or other CNS depressants, including sedating antidepressants, antipsychotics, or anti-epileptics; opioids; benzodiazepines; muscle relaxants; and general anesthetics
 - The risks of operating hazardous machinery, including automobiles or airplanes, for the first 6 hours after taking a dose of sodium oxybate
 - Preparation and dosing instructions for sodium oxybate
 - The risk of abuse and misuse associated with sodium oxybate
 - Safe use, handling, and storage of sodium oxybate (refer to pages 13 & 14 of this brochure for Patient Counseling Information)
 - 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. This can be done by completing the Medications field on the *Sodium Oxybate REMS Program Prescription Form* or by faxing a separate page from the patient's medical history

NOTE: Prior to dispensing each sodium oxybate prescription (including refills), the certified pharmacy responsible to dispense sodium oxybate to the patient will complete a Drug Utilization Review (DUR) and, during the patient counseling process, will ask the patient about the use of other medicines. If the patient's certified pharmacy learns that the patient is taking a previously undisclosed contraindicated medication (sedative hypnotics), an opioid, or more than one CNS depressant, and the prescriber has not indicated awareness of the concomitant medication, the patient's certified pharmacy will contact and inform the prescriber of the concomitant medication use prior to dispensing sodium oxybate. The patient's certified pharmacy may also contact the prescriber about other concomitant medications of concern.

PRESCRIBING SODIUM OXYBATE A BRIEF GUIDE (CONT'D)

- Verify that you have informed the patient that his or her certified pharmacy will send him/her a copy of the sodium oxybate Medication Guide with each prescription fill and a *Sodium Oxybate REMS Program Patient Quick Start Guide* prior to his/her first prescription fill, if you haven't provided one previously. These materials are available through the Sodium Oxybate REMS Program at www.SodiumOxybateREMSProgram.com
- Access www.SodiumOxybateREMSProgram.com to look up the certified pharmacies
- Fax the completed *Sodium Oxybate REMS Program Prescription Form* and all renewal/refill prescriptions to one of the certified pharmacies

Patient Evaluation

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

Refill Prescriptions

- One of the certified pharmacies will send you a *Sodium Oxybate REMS Program Prescription Form* in advance of a patient's prescription expiring or running out of refills. Prescription refills and renewals may also be conveyed by phone or fax to the patient's certified pharmacy, and must be documented in the Sodium Oxybate REMS Program.
 - Fill out the form completely and clearly to ensure timely fulfillment of your patient's prescription
 - Access www.SodiumOxybateREMSProgram.com to look up the certified pharmacies
 - Fax the completed *Sodium Oxybate REMS Program Prescription Form* and all subsequent prescriptions to one of the certified pharmacies

RESPONSIBILITIES OF THE SODIUM OXYBATE REMS PROGRAM CERTIFIED PHARMACIES

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

- Provide you with confirmation of each new *Sodium Oxybate REMS Program Prescription Form* received from your office
- Contact the patient's insurance provider to verify sodium oxybate prescription benefits
- Prior to the first shipment, contact the patient to:
 - Confirm whether he or she has received a copy of the *Sodium Oxybate REMS Program Patient Quick Start Guide*. The patient's certified pharmacy will send a copy of the *Sodium Oxybate REMS Program Patient Quick Start Guide* to any patient not previously receiving one from his or her prescriber
 - Counsel the patient using the *Sodium Oxybate REMS Program Patient Counseling Checklist* on expectations from sodium oxybate therapy and how to prepare and take sodium oxybate doses safely and effectively
 - Review important sodium oxybate safety information and precautions for sodium oxybate use
 - Review sodium oxybate safe handling and storage procedures
 - Review the adverse events associated with sodium oxybate
 - Review the patient's use of concomitant medications
 - You will be notified of any potential for drug interactions based on patient counseling
 - Ask if the patient has any questions about sodium oxybate 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 sodium oxybate by overnight service to the patient or his or her authorized adult designee
- Remind patients about monthly refills
- Contact the prescriber if a prescription refill or renewal is required

For your convenience, materials and information regarding the Sodium Oxybate REMS Program are available online at www.SodiumOxybateREMSProgram.com.

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

GUIDELINES FOR DOSING AND TITRATING SODIUM OXYBATE

DOSING SODIUM OXYBATE

Sodium oxybate is a liquid medication taken orally at bedtime. Due to its short half-life, sodium oxybate is taken in 2 equal doses at night, with the first dose taken at bedtime and the second dose taken 2.5 to 4 hours later.

- **The recommended starting dose is 4.5 g/night divided into 2 equal doses of 2.25 g each**
- The effective dose range is 6 g to 9 g/night
- Doses higher than 9 g/night have not been studied and should not ordinarily be administered
- The dose of sodium oxybate should be titrated to effect
 - Sodium oxybate should be titrated in increments of 1.5 g/night at weekly intervals
- An initial sodium oxybate dose reduction of at least 20% is recommended if divalproex sodium is prescribed to patients already taking sodium oxybate. For patients already taking divalproex sodium, it is recommended that prescribers use a lower starting sodium oxybate dose when introducing sodium oxybate. Prescribers are advised to monitor patient response closely and adjust dose accordingly if concomitant use of sodium oxybate and divalproex sodium is warranted
- Improvement may occur during the first weeks of therapy; however, titration to an optimal dose may take longer
- Once a stable dose is established, patients should be evaluated periodically

Note: the patient's first shipment of sodium oxybate will be limited to a 1-month (30-day) supply, and future shipments cannot exceed a 3-month (90-day) supply.

DOSING AND TITRATION			
	1 st Dose	2 nd Dose	Total Nightly Dose
Recommended Starting Dose	2.25 g	2.25 g	4.5 g
	3 g	3 g	6 g
	3.75 g	3.75 g	7.5 g
Maximum Dose	4.5 g	4.5 g	9 g
			Effective Dosing Range

Please see PI for sodium oxybate for additional guidelines for dosing and titration.

PATIENT DOSING INFORMATION:

- Inform patients that all bottles contain concentrated medication ONLY and that water for dilution is not contained in the box. Advise patients to keep sodium oxybate in the provided bottle(s)
- Patients should prepare both nighttime doses at bedtime
 - Instruct patients to make sure that pharmacy vials are empty prior to preparing each dose
 - Each dose of sodium oxybate should be diluted with about 1/4 cup of water
 - Patients should be instructed to store sodium oxybate bottles and prepared nightly doses in a secure place out of the reach of children and pets
- Food significantly reduces the bioavailability of sodium oxybate; therefore, **doses should be taken at least 2 hours after eating**
- Both doses should be taken while in bed
- The first dose should be taken at bedtime and the second dose 2.5 to 4 hours later

ADDITIONAL INFORMATION ABOUT SODIUM OXYBATE

Sodium oxybate has been placed in a bifurcated federal schedule. Sodium oxybate is a Schedule III controlled substance when used for legitimate medical purposes, as prescribed. The active ingredient, sodium oxybate, or gamma-hydroxybutyrate (GHB), is classified as a Schedule I controlled substance when used for any other reason or by anyone other than for whom it was prescribed. Your patients should be informed that federal law prohibits the transfer of sodium oxybate to any persons other than the patient for whom it was prescribed. If you have any questions regarding this, please call the Sodium Oxybate REMS Program toll-free at 855-705-2424.

Illicit use and abuse of GHB have been reported, including drug-facilitated sexual assault. 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 dose or frequency of dosing, reports of lost, stolen, or spilled medication, drug-seeking behavior).

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 that there is potential to abuse sodium oxybate

It is important you know that the Sodium Oxybate REMS Program maintains records about who is prescribing sodium oxybate. These records will be made available to any state or federal agency that requests them.

DEPENDENCE AND TOLERANCE

Dependence

- Cases of severe dependence and cravings for GHB have been reported
- There have been case reports of dependence after illicit use of GHB at frequent repeated doses
 - Doses (18 g/day to 250 g/day) were in excess of therapeutic dose range
- Abstinence syndrome has not been reported in clinical trials

Tolerance

- Open-label, long-term (≥6 months) clinical trials did not demonstrate development of tolerance
- There have been some case reports of symptoms of tolerance developing after illicit use at doses far in excess of the recommended sodium oxybate dosage regimen

Discontinuation effects and tolerance of sodium oxybate have not been systematically evaluated in controlled clinical trials.

For your convenience, materials and information regarding the Sodium Oxybate REMS Program are available online at www.SodiumOxybateREMSProgram.com

USE IN SPECIFIC POPULATIONS

PREGNANCY

Teratogenic Effects: Pregnancy Category C.

Nonteratogenic Effects: Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

LABOR AND DELIVERY

Sodium oxybate 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, but umbilical vein levels of sodium oxybate were no more than 25% of the maternal concentration. No sodium oxybate was detected in the infant's blood 30 minutes after delivery. Elimination curves of sodium oxybate between a 2-day-old infant and a 15-year-old patient were similar. Subsequent effects of sodium oxybate on later growth, development, and maturation in humans are unknown.

NURSING MOTHERS

It is not known whether sodium oxybate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when sodium oxybate is administered to a nursing woman.

PEDIATRIC USE

Safety and effectiveness in pediatric patients have not been established.

GERIATRIC USE

There is limited experience with sodium oxybate in subjects 65 years and older. 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 and other drug therapy.

RACE AND GENDER EFFECTS

There were too few non-Caucasian patients in the narcolepsy clinical trials to permit evaluation of racial effects on safety or efficacy. More than 90% of the subjects in the clinical trials were Caucasian.

In the narcolepsy clinical trials, with a database that was 58% female, no important differences in safety or efficacy of sodium oxybate were noted between men and women.

Please read accompanying Prescribing Information.

The Sodium Oxybate REMS Program is here to support you, your staff, and your patients.

For assistance, call 855-705-2424 (toll-free).

PATIENT COUNSELING INFORMATION

Prior to initiating therapy, counsel each patient regarding the serious risks and safe use, handling and storage of sodium oxybate using the *Sodium Oxybate REMS Program Patient Quick Start Guide* and encourage all patients to read the sodium oxybate Medication Guide.

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

As a component of the Sodium Oxybate REMS Program, the contents of the sodium oxybate Medication Guide are reviewed with every patient by a Sodium Oxybate REMS Program certified pharmacy before initiating treatment with sodium oxybate.

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

ALCOHOL OR SEDATIVE HYPNOTICS

Advise patients not to drink alcohol or take other sedative hypnotics if they are taking sodium oxybate.

SEDATION

Inform patients that after taking sodium oxybate they are likely to fall asleep quickly (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 their first dose, and not to take their second dose until 2.5 to 4 hours later.

FOOD EFFECTS ON SODIUM OXYBATE

Food significantly decreases the bioavailability of sodium oxybate. Inform patients to take the first dose at least 2 hours after eating.

RESPIRATORY DEPRESSION

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

OPERATING HAZARDOUS MACHINERY

Inform patients that until they are reasonably certain that sodium oxybate does not affect them adversely (e.g., impair judgment, thinking, or motor skills) they should not operate hazardous machinery, including automobiles or airplanes.

SUICIDALITY

Instruct patients or families 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 and their families that sodium oxybate has been associated with sleepwalking and to contact their healthcare provider if this occurs.

SODIUM INTAKE

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

SAFE USE, HANDLING, STORAGE, AND DISPOSAL

- Discuss safe and proper use of sodium oxybate and dosing information with patients prior to the initiation of treatment
- Instruct patients to store sodium oxybate bottles and sodium oxybate doses in a secure place, out of reach of children and pets
- Patients should be instructed to divide their total nightly dose into 2 separate doses. They should not further divide each of the 2 separate doses
- Patients should be informed that they should be seen by their healthcare provider frequently to review dose titration, symptom response, and adverse reactions
- Instruct patients to store sodium oxybate at room temperature, between 59°F and 86°F. Inform patients that they may safely dispose of sodium oxybate down the sink or toilet drain
- Inform patients that they must report all instances of lost or stolen sodium oxybate to the local police and to the Sodium Oxybate REMS Program