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## Introduction

- Low-sodium oxybate (LXB; Xywav<sup>®</sup>) and high-sodium oxybate (SXB; Xyrem<sup>®</sup>) are approved in the United States to treat cataplexy or excessive daytime sleepiness in patients  $\geq 7$  years of age with narcolepsy<sup>1-5</sup>; LXB is also approved for idiopathic hypersomnia in adults<sup>2</sup>
- LXB and SXB are available through the same manufacturer's Risk Evaluation and Mitigation Strategy (REMS) under the US Food and Drug Administration<sup>6</sup>
  - Patients and prescribers receive training and educational materials about significant risks, safe handling, and storage of LXB and SXB, along with information about the requirements of the REMS
  - Additionally, prescribers receive education on appropriate prescribing indications
- Knowledge, attitude, and behavior (KAB) surveys were conducted to document and assess patient and prescriber awareness of the information communicated through the REMS

## Objective

- To assess the outcomes from the KAB surveys of patient and prescriber understanding of serious risks, safe use, and proper handling of LXB and SXB, as well as REMS requirements

## Methods

- Patient participants were  $\geq 18$  years of age, had filled a prescription for LXB or SXB in the prior 6 months, and were identified as enrolled in the REMS
- Prescriber participants were US-based, had prescribed LXB or SXB to  $\geq 1$  patient in the prior 12 months, and were identified as enrolled in the REMS
- All patient and prescriber participants in the REMS database meeting inclusion criteria and none of the exclusion criteria were invited to participate
- Considering LXB and SXB jointly, survey questions were designed to evaluate if prescribers could correctly identify the prescribing indications, and whether patients and prescribers were aware of the following:
  - Risks of central nervous system and respiratory depression
  - Contraindications with sedative hypnotics and/or alcohol
  - The potential for abuse, misuse, and overdose
  - Appropriate dosing and safe handling
  - Requirements of the REMS for LXB and SXB

## Results

- Internet, telephone, and paper surveys were conducted between October 27, 2022, and February 26, 2023

**Table 1. Prescribers Identified Indications**

Question	Correct Choice	Respondents, n/N* (%)
<b>Which of the following are approved indications for LXB and/or SXB?</b>		
Cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy	Yes	250/273 (91.6)
Insomnia in patients 7 years of age and older	No	211/273 (77.3)
Idiopathic hypersomnia in adults	Yes	235/269 (87.4)

Percentages are calculated based on the number not missing for each question. Results represent respondents who made a correct choice.  
\*Number not missing.  
LXB, low-sodium oxybate; SXB, high-sodium oxybate.

**Table 2. Patients and Prescribers Were Aware of Risks of CNS and Respiratory Depression**

Patients			Prescribers		
Question	Correct Choice	Respondents, n (%)	Question	Correct Choice	Respondents, n (%)
<b>Which of the following are risks related to taking LXB/SXB at recommended doses? Select all that apply</b>			<b>Which of the following are risks related to taking LXB/SXB at recommended doses? Select all that apply</b>		
Passing out or fainting	<input checked="" type="checkbox"/>	1436 (45.6)	CNS depression	<input checked="" type="checkbox"/>	250 (91.6)
Trouble breathing while asleep	<input checked="" type="checkbox"/>	2358 (74.8)	Respiratory depression	<input checked="" type="checkbox"/>	217 (79.5)

Percentages are calculated based on the number not missing for each question. Results represent respondents who made a correct choice.  
\*Number not missing.  
CNS, central nervous system; LXB, low-sodium oxybate; SXB, high-sodium oxybate.

**Table 3. Patients and Prescribers Identified the Risks of Abuse, Misuse, and Overdose**

Patients			Prescribers		
Question	Correct Choice	Respondents, n (%)	Question	Correct Choice	Respondents, n (%)
There is a risk of abusing LXB/SXB	True	2790 (89.6)	There is a risk of abusing LXB/SXB	True	249 (91.2)
<b>Which of the following are risks related to taking too much LXB/SXB? Select all that apply</b>		N=3102*	<b>Which of the following are risks that have been associated with overdosing on LXB/SXB? Select all that apply</b>		
Unwanted changes in alertness or drowsiness	<input checked="" type="checkbox"/>	2471 (79.7)	Coma	<input checked="" type="checkbox"/>	197 (72.2)
Death	<input checked="" type="checkbox"/>	2454 (79.1)	Death	<input checked="" type="checkbox"/>	221 (81.0)
Trouble breathing	<input checked="" type="checkbox"/>	2645 (85.3)	Respiratory depression	<input checked="" type="checkbox"/>	266 (97.4)
Blindness or loss of vision	<input type="checkbox"/>	198 (6.4)	Cardiomyopathy	<input type="checkbox"/>	19 (7.0)
<b>Using LXB/SXB for fun, such as using it to feel "high," may lead to dependence</b>	True	2237 (72.2)	<b>Which of the following could be indicators of inappropriate use (in other words, abuse, misuse, diversion) of LXB/SXB? Select all that apply</b>		
Abusing LXB/SXB may cause serious medical problems	True	2911 (93.9)	A pattern of reporting lost, stolen, destroyed, or spilled medication	<input checked="" type="checkbox"/>	270 (99.3)
It is ok to take a higher dose of LXB/SXB than prescribed	False	3056 (98.6)	Drug-seeking behavior	<input checked="" type="checkbox"/>	263 (96.7)
It is ok to take two doses of LXB/SXB at the same time	False	3021 (97.5)	Requests to reduce the size or frequency of dosing	<input type="checkbox"/>	32 (11.8)

Percentages are calculated based on the number not missing for each question. Regular text represents respondents who made a correct choice. Italicized font indicates that an incorrect choice was made.  
\*Number not missing.  
LXB, low-sodium oxybate; SXB, high-sodium oxybate.

**Table 5. Patients and Prescribers Identified REMS Requirements**

Patients			Prescribers		
Question	Correct Choice	Respondents, n/N* (%)	Question	Correct Choice	Respondents, n (%)
<b>Patients should discuss the safe use of LXB/SXB with their healthcare provider</b>	True	3063/3088 (99.2)	<b>Which of the following are prescribers expected to counsel LXB/SXB patients about? Select all that apply</b>		
<b>Patients should tell their healthcare provider if they take any medicines or have any medical conditions that may affect their breathing</b>	True	3059/3088 (99.1)	The risks of concomitant use of LXB/SXB with alcohol, other CNS depressants, and other contraindications	<input checked="" type="checkbox"/>	266 (98.9)
<b>Patients should read the Patient Quick Start Guide before they begin taking LXB/SXB</b>	True	3059/3088 (99.1)	Preparation and dosing instructions for LXB/SXB	<input checked="" type="checkbox"/>	255 (94.8)
<b>Patients should be aware of the risks of LXB/SXB</b>	True	3087/3088 (100.0)	The risks of doing hazardous activities requiring complete alertness or coordination for 6 hours after taking LXB/SXB	<input checked="" type="checkbox"/>	261 (97.0)
<b>LXB/SXB patients are required to be enrolled in a special safety program called a REMS program</b>	True	2175/3084 (70.5)	The risks of abusing LXB/SXB	<input checked="" type="checkbox"/>	261 (97.0)
			The safe and appropriate use, handling, and storage of LXB/SXB	<input checked="" type="checkbox"/>	255 (94.8)
			<b>Which one of the following statements about the responsibilities of LXB/SXB prescribers is true? Select 1 response</b>		
			Prescribers agree to evaluate each patient within the first 3 months of starting LXB/SXB	<input checked="" type="checkbox"/>	232 (86.2)
			A history of alcohol or substance abuse	<input checked="" type="checkbox"/>	267 (98.9)
			Enrollment in the LXB/SXB REMS <sup>®</sup> is optional for prescribers	<input type="checkbox"/>	18 (6.7)
			A history of sleep-related breathing disorders	<input checked="" type="checkbox"/>	255 (94.4)
			Prescribers must order laboratory tests to be sent to the certified pharmacy	<input type="checkbox"/>	5 (1.9)
			A history of compromised respiratory function	<input checked="" type="checkbox"/>	252 (93.3)
			<b>Prescribers are expected to report an occurrence of a potential serious adverse event experienced by a patient taking LXB/SXB to</b>		
			Jazz Pharmaceuticals	Yes	264 (98.1)
			Concomitant use of agents that may interact with LXB/SXB	<input checked="" type="checkbox"/>	265 (98.1)
			A history of depression or suicidality	<input checked="" type="checkbox"/>	258 (95.6)

Percentages are calculated based on the number not missing for each question. Regular text represents respondents who made a correct choice. Italicized font indicates that an incorrect choice was made.  
\*Number not missing.  
<sup>®</sup>Actual name in survey was XYWAV/XYREM REMS.  
CNS, central nervous system; LXB, low-sodium oxybate; REMS, Risk Evaluation and Mitigation Strategy; SXB, high-sodium oxybate.

**Table 4. Patients and Prescribers Understood Dosing, Storage, and Safe Handling**

Patients			Prescribers		
Question	Correct Choice	Respondents, n (%)	Question	Correct Choice	Respondents, n (%)
Patients should take the first dose of LXB/SXB at bedtime	True	3080 (99.5)	Patients should take the first dose of LXB/SXB at bedtime	True	268 (98.9)
Patients should take the second dose (if prescribed) of LXB/SXB 2.5 hours to 4 hours after the first dose	True	3064 (99.0)	Patients should take the second dose (if prescribed) of LXB/SXB 2.5 hours to 4 hours after the first dose	True	268 (98.9)
Patients should stay in bed after taking LXB/SXB	True	3077 (99.4)	Patients should stay in bed after taking LXB/SXB	True	260 (95.9)
Patients should avoid driving or using heavy machinery for 6 hours after taking LXB/SXB	True	3023 (97.6)			
			<b>Patient Only</b>		
Patients should mix LXB/SXB with water	True	3075 (99.3)			
<b>Which of the following are true about the proper storage of LXB/SXB? Select all that apply</b>		N=3095*	<b>Which of the following are true about the proper storage of LXB/SXB? Select all that apply</b>		
LXB/SXB should be stored in its original bottle	<input checked="" type="checkbox"/>	3010 (97.3)	LXB/SXB should be prepared and stored in the containers provided by the pharmacy	<input checked="" type="checkbox"/>	231 (85.2)
LXB/SXB and prepared doses should be stored in a safe place, out of the reach of children and pets	<input checked="" type="checkbox"/>	3029 (97.9)	LXB/SXB and prepared doses should be stored in a safe place, out of the reach of children and pets	<input checked="" type="checkbox"/>	257 (94.8)
LXB/SXB should be stored in the refrigerator	<input type="checkbox"/>	21 (0.7)	LXB/SXB should be stored in the refrigerator	<input type="checkbox"/>	47 (17.3)
<b>Safe handling of LXB/SXB</b>		N=3093*	<b>Safe handling of LXB/SXB</b>		
It is against the law for patients to give or sell LXB/SXB to another person, even someone with the same symptoms	True	3059 (98.9)	It is against the law for patients to give or sell LXB/SXB to another person, even someone with the same symptoms	True	270 (99.6)
If the patient's LXB/SXB is lost or stolen, they should tell the local police and the LXB/SXB dispensing pharmacy	True	2771 (89.6)	If the patient's LXB/SXB is lost or stolen, they should tell the local police and the LXB/SXB dispensing pharmacy	True	237 (87.5)

Percentages are calculated based on the number not missing for each question. Regular text represents respondents who made a correct choice. Italicized font indicates that an incorrect choice was made.  
\*Number not missing.  
LXB, low-sodium oxybate; SXB, high-sodium oxybate.

**Table 6. Patients and Prescribers Identified Contraindications**

Patients			Prescribers		
Question	Correct Choice	Respondents, n (%)	Question	Correct Choice	Respondents, n (%)
<b>Is there a risk of serious side effects if you use LXB/SXB together with the following?</b>			<b>LXB/SXB is contraindicated for use in:</b>		
Other medicines that cause sleepiness	Yes	2966 (95.1)	Patients treated with sedative hypnotics (for example, Ambien <sup>®</sup> /zolpidem or Sonata <sup>®</sup> /zaleplon)	True	240 (87.9)
Alcohol (for example, beer, wine, or liquor)	Yes	3028 (97.1)	Combination with alcohol	True	264 (96.7)

Percentages are calculated based on the number not missing for each question. Results represent respondents who made a correct choice.  
\*Number not missing.  
LXB, low-sodium oxybate; SXB, high-sodium oxybate.

## Conclusions

- The majority of patients and prescribers surveyed demonstrated understanding of the serious risks, dosing instructions, and safe handling of LXB and SXB
- A possible limitation of the survey is the self-selection process, as patients who chose to respond to the invitation may differ in their understanding of the important safety information from those who elected to not participate
- Results also demonstrate that the majority of patients and prescribers surveyed understood the requirements of the REMS for LXB and SXB

**References:** 1. Xyrem<sup>®</sup> (sodium oxybate) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. 2. Xywav<sup>®</sup> (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. 3. Szarfman A, et al. *N Engl J Med*. 1995;333(19):1291. 4. US Food and Drug Administration. Clinical review for Binosto, NDA 202344. 2012. [https://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2012/202344Orig1s000MedR.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202344Orig1s000MedR.pdf). Accessed February 28, 2023. 5. US Food and Drug Administration. Quantitative labeling of sodium, potassium, and phosphorus for human over-the-counter and prescription drug products. Guidance for industry. 2022. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/quantitative-labeling-sodium-potassium-and-phosphorus-human-over-counter-and-prescription-drug>. Accessed October 11, 2022. 6. Xywav and Xyrem REMS prescriber brochure. 2021. <https://www.xywavxyremrems.com/>. Accessed February 21, 2023.

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