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Insights From Real-World and Interventional Studies of Patients Transitioning From Sodium Oxybate to Low-Sodium Oxybate

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Introduction

- Low-sodium oxybate (LXB; Xywav®) contains the same active moiety as sodium oxybates (sodium oxybate [SXB; Xyrem®] and fixed-dose, sodium oxybate [Lumryz™]), but with 92% less sodium, and is approved by the US Food and Drug Administration (FDA) for treating cataplexy or excessive daytime sleepiness in patients ≥7 years of age with narcolepsy[1-5]
  - LXB has been recognized by the US FDA in the narcolepsy population for its significant reduction in chronic sodium burden compared with sodium oxybate products and formulations, which "will be clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated"[6]
- One real-world and 1 interventional study have examined the experience of adults with narcolepsy (type 1 or type 2) transitioning to LXB from SXB (Transition Experience of persons with Narcolepsy taking Oxybate in the Real-world [TENOR], NCT04803786; Substitution of Equal Grams of Uninterrupted Xyrem® to Xywav® [SEGUE]; NCT04794491)

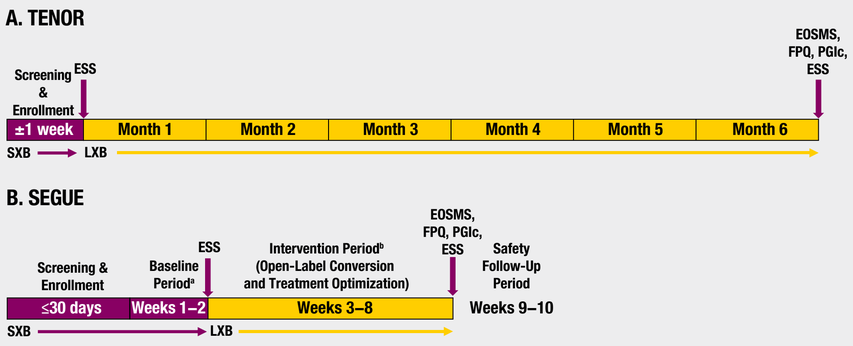
Objective

- Describe treatment satisfaction and effectiveness, and patient preferences, among adults with narcolepsy (type 1 or type 2) transitioning to LXB from SXB in TENOR and SEGUE

Methods

- TENOR was a 21-week, prospective, observational, virtual-format study; SEGUE was an 8-week, multicenter, interventional, site-based study
- TENOR participants were transitioning to LXB from SXB within the previous/upcoming 7 days; in SEGUE, after 2 weeks on a stable SXB dose/regimen (baseline period), participants switched to the same dose/regimen of LXB and were titrated if needed (intervention period; 6 weeks)
- Participants in both studies responded to questionnaires including the Patient Global Impression of Change (PGIc), a forced preference questionnaire (FPQ), an ease of switching medication scale (EOSMS), and the Epworth Sleepiness Scale (ESS)
  - PGIc asks participants to rate their excessive daytime sleepiness (TENOR) or overall narcolepsy symptoms (SEGUE) on a 7-point Likert-type scale from "Very much improved" to "Very much worse"
  - FPQ asks "Thinking about your experience with Xyrem and Xywav, which would you prefer to treat your narcolepsy?"
  - EOSMS prompts participants to rate the process of switching to the new medication on a 5-point Likert-type scale from "Extremely easy, not difficult at all," to "Extremely difficult, not easy at all"
  - ESS asks participants to rate the likelihood of falling asleep in various scenarios; scale range 0–24[7]

Figure 1. Study Design



[a]Participants were taking a stable dose of SXB (with or without concomitant anticataplectics or stimulants).
[b]Participants converted from SXB to LXB (gram-for-gram); if needed, they were titrated to stable dose and regimen. Dose/regimen of any concomitant anticataplectics or stimulants were maintained.
EOSMS, ease of switching medication scale; ESS, Epworth Sleepiness Scale; FPQ, forced preference questionnaire; LXB, low-sodium oxybate; PGIc, Patient Global Impression of Change; SXB, sodium oxybate.

Results

Table 1. Participant Demographics

	TENOR (N=85)	SEGUE (N=62)
Age, mean (SD), years	40 (13.0)	44.3 (15.2)
Female, n (%)	62 (72.9)	37 (59.7)
Race, n (%)		
American Indian or Alaska Native	3 (3.5)	0
Asian	4 (4.7)	2 (3.2)
Black or African American	6 (7.1)	6 (9.7)
White	74 (87.1)	54 (87.1)
Other	5 (5.9)	0

SD, standard deviation.

Table 2. SXB Dosing Regimen

	TENOR (N=85)	SEGUE (N=62)
Prescribed SXB doses/night, n (%)		
Twice	82 (96.5)	58 (93.5)
Other[a]	3 (3.5)	4 (6.5)
Total nightly SXB dose, mean (SD), g	7.7 (1.5)	8.0 (1.4)

[a]Includes participants who took SXB once or three times nightly (as reported by participants in TENOR, or as prescribed by physicians in SEGUE).
SD, standard deviation; SXB, sodium oxybate.

- Nearly all participants (92%) in TENOR achieved a stable dose of LXB during study week 5; most participants (83%) reported that they did not change their usual LXB dosing routines during the final week of the study
- Nearly all participants (93%) in SEGUE achieved a stable dose of LXB by study week 8; most participants' physicians (89%) never initiated changes to participants' dosing regimens

Figure 2. Most Participants Indicated That the Process of Switching From SXB to LXB Was Easy

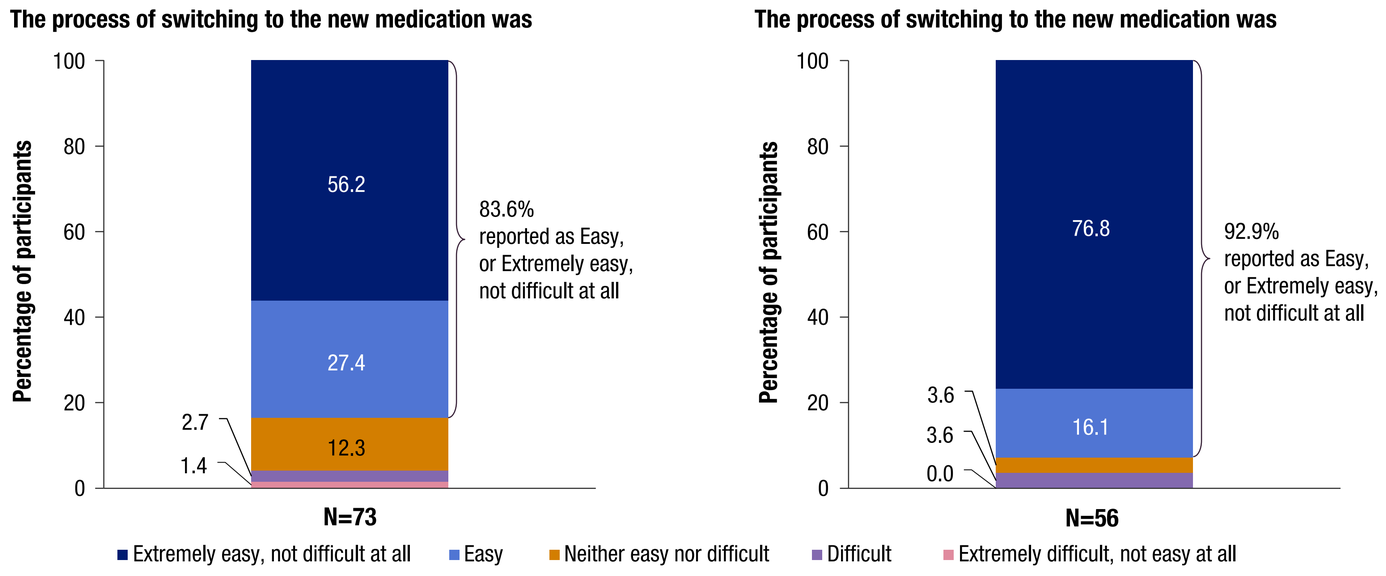
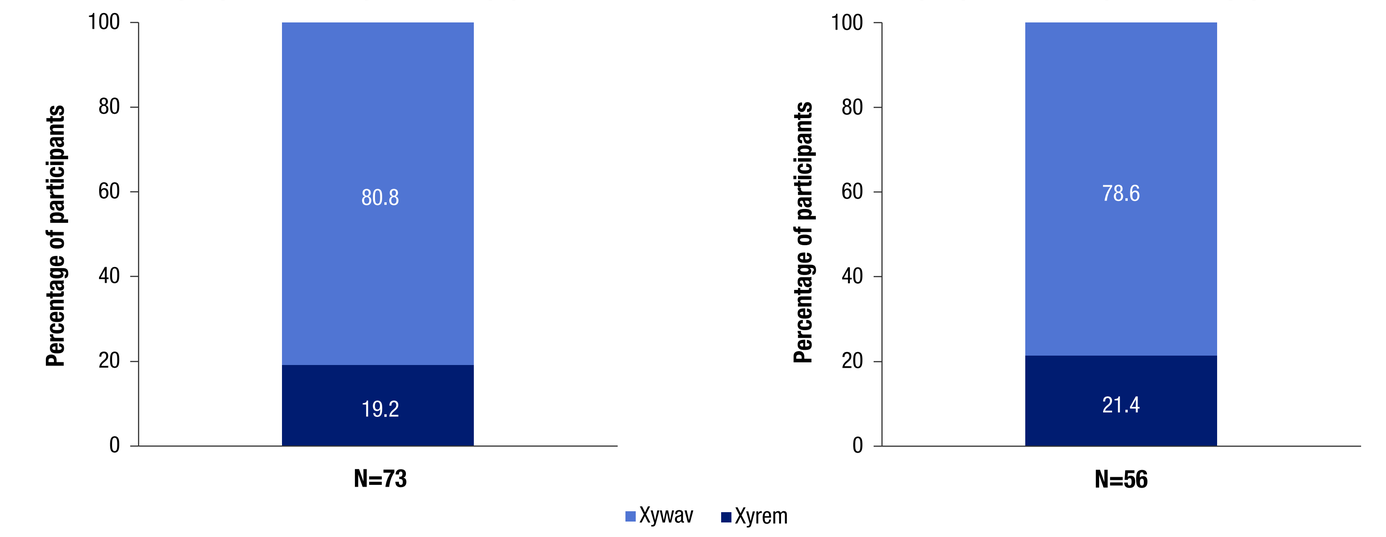
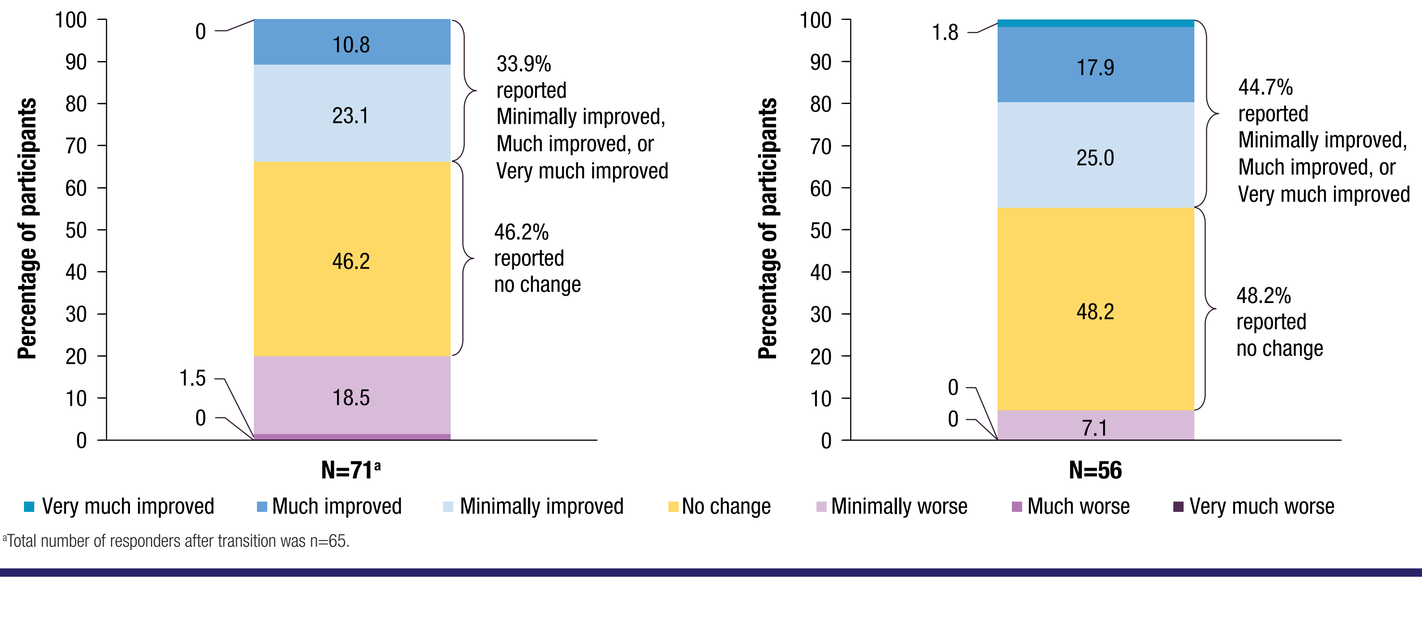


Figure 3. Most Participants Preferred LXB to SXB



- In both studies, the most commonly reported reason for preferring SXB was related to taste, whereas most participants who preferred LXB did so for its lower sodium content

Figure 4. Most Participants Reported Improvement or No Change in Symptoms After Transitioning From SXB to LXB



[a]Total number of responders after transition was n=65.

Table 3. ESS Scores Were Maintained After Transitioning From SXB to LXB

	SXB (Baseline)		LXB (End of study[a]/intervention period[b])		Change from baseline	
	TENOR	SEGUE	TENOR	SEGUE	TENOR	SEGUE
N	**84**	**59**	**68**	**56**	**68**	**55**
Mean (SD)	9.9 (5.2)	9.4 (4.9)	7.5 (4.7)	8.8 (5.1)	–2.0 (3.8)	–0.7 (2.3)
Median (min, max)	9.0 (0, 22)	9.0 (1, 20)	7.0 (0, 19)	8.0 (1, 23)	–2.0 (–16, 7)	0.0 (–8, 4)

[a]TENOR.
[b]SEGUE; includes participants who completed the end of treatment or early discontinuation visit.
ESS, Epworth Sleepiness Scale; LXB, low-sodium oxybate; max, maximum; min, minimum; SD, standard deviation; SXB, sodium oxybate.

Limitations

- Interpretation of these combined results is complicated by differences in study designs and methodologies of TENOR and SEGUE
- These results are based on subjective participant self-reports

Conclusions

- Most participants across both studies (TENOR and SEGUE) reported that switching to LXB from SXB was easy with minimal modifications to dose/regimen
- The majority of participants who self-reported a preference for LXB cited lower sodium content as the reason
- Across both studies, there were no clinically meaningful changes in ESS scores, and a majority of participants reported that their excessive daytime sleepiness (TENOR) or narcolepsy symptoms (SEGUE) were unchanged or improved following transition from SXB to LXB, suggesting that treatment effectiveness was maintained

References: 1. Bogan RK, et al. *Sleep*. 2021;44:zsaa206. **2.** Xyrem® (sodium oxybate) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2023. **3.** Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2023. **4.** Lumryz™ (sodium oxybate) for extended-release oral solution, CIII [prescribing information]. Chesterfield, MO: Avadel CNS Pharmaceuticals; 2023. **5.** Szarfman A, et al. *N Engl J Med*. 1995;333:1291. **6.** Clinical superiority findings. 2021. Available at: https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/clinical-superiority-findings. **7.** Johns MW. *Sleep*. 1991;14:540-5.

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