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# Effectiveness and Optimization of Low-Sodium Oxybate in Participants With Narcolepsy Switching From Sodium Oxybate (SEGUE)

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## Introduction

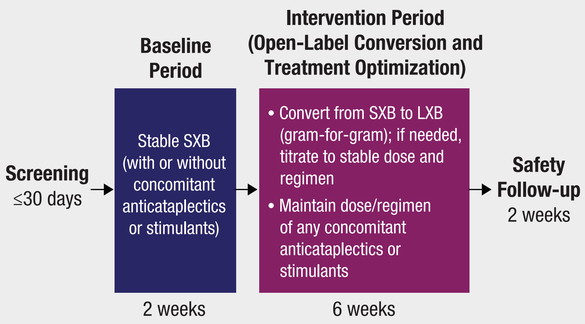
- Sodium oxybate (SXB; Xyrem®) is strongly recommended by the American Academy of Sleep Medicine for the treatment of narcolepsy due to its efficacy in improving cataplexy and excessive daytime sleepiness[1]
- Low-sodium oxybate (LXB; Xywav®), which contains the same active moiety as high-sodium oxybates (SXB and fixed-dose, high-sodium oxybate [Lumryz™]), but with 92% less sodium, 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, and idiopathic hypersomnia in adults[2-7]
  - LXB has been recognized by the US FDA in the narcolepsy population for its significant reduction in chronic sodium burden compared with high-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"[8]
- SEGUE (Substitution of Equal Grams of Uninterrupted Xyrem® to Xywav®) was a phase 4, multicenter, open-label, single-arm study of safety, tolerability, effectiveness, and treatment optimization in participants with narcolepsy transitioning from SXB to LXB (NCT04794491)

## Objective

- The primary objective of this study was to describe the clinical experience of participants switching from SXB to LXB for the treatment of narcolepsy with or without cataplexy
- An exploratory objective was to describe the ease of conversion and participant preference for LXB

## Methods

**Figure 1. SEGUE Study Design**




LXB, low-sodium oxybate; SXB, sodium oxybate.

- Eligible participants were adults 18 to 80 years of age with narcolepsy type 1 or type 2 (based on criteria from the *International Classification of Sleep Disorders*, 3rd Edition[9] or *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition[10]) who had been taking a stable dose (maximum 9 g/night; no single dose >6 g) and regimen (once, twice, or thrice nightly) of SXB for ≥2 months, with or without additional anticataplectics or stimulants
- After 2 weeks on a stable SXB dose/regimen (baseline period), participants switched to the same dose (gram-for-gram) and regimen of LXB; any concomitant anticataplectics or stimulants were maintained at the current dose and regimen (intervention period; 6 weeks)
  - If required, LXB dose and regimen were titrated to optimize efficacy and tolerability
- Efficacy assessments included 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),[11] all collected at the end of treatment or early discontinuation
- Treatment-emergent adverse events (TEAEs), as reported by participants, were collected until the end of the safety follow-up

## Results

**Table 1. Scores on the ESS Were Similar at the End of the Intervention Period Compared With Baseline**

| ESS Score | SXB Baseline (Day 1) | LXB End of Intervention Period[a] | Change |
|---|---|---|---|
| n | 59 | 56 | 55 |
| Mean (SD) | 9.4 (4.9) | 8.8 (5.1) | –0.7 (2.3) |
| Median (min, max) | 9.0 (1, 20) | 8.0 (1, 23) | 0.0 (–8, 4) |

[a]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.

**Table 2. Most Participants Kept the Same Dose and Regimen After Switching From SXB to LXB Gram-for-Gram**

| Parameter | Participants[a] N=56 |
|---|---|
| **Time to achieve stable LXB dose and regimen[b,c], days** | |
| Mean (SD) | 2.5 (4.8) |
| Median (min, max) | 1.0 (1, 28) |
| **Number of changes required to achieve stable LXB dose and regimen** | |
| Mean (SD) | 0.1 (0.3) |
| Median (min, max) | 0.0 (0, 1) |
| No changes, n (%) | 50 (89.3) |
| Changed once, n (%) | 6 (10.7) |
| Changed ≥2 times, n (%) | 0 (0) |

[a]Participants with LXB dose and regimen unchanged from Visit 7 or earlier to Visit 8, or the final dose and regimen remain the same for ≥2 weeks for participants who early terminated LXB treatment. Four participants did not reach a stable dose due to early termination from the study (2 participants because of protocol violations; 1 participant following an adverse event; 1 participant after withdrawal of consent). [b]Defined as the time from the first dose and regimen of LXB to the stable dose and regimen of LXB. [c]For participants who did not change their LXB dose and regimen, the minimum value (1 day) was noted.
LXB, low-sodium oxybate; max, maximum; min, minimum; SD, standard deviation; SXB, sodium oxybate.

**Table 3. Baseline Demographics**

| Characteristic | Safety Population[a] (N=62) |
|---|---|
| **Age, years** | |
| Mean (SD) | 44.3 (15.2) |
| Median (min, max) | 41.5 (18, 74) |
| **Sex, n (%)** | |
| Male | 25 (40.3) |
| Female | 37 (59.7) |
| **Race, n (%)** | |
| Asian | 2 (3.2) |
| Black or African American | 6 (9.7) |
| White | 54 (87.1) |
| **Ethnicity, n (%)** | |
| Hispanic or Latino | 4 (6.5) |
| Non-Hispanic or Latino | 58 (93.5) |

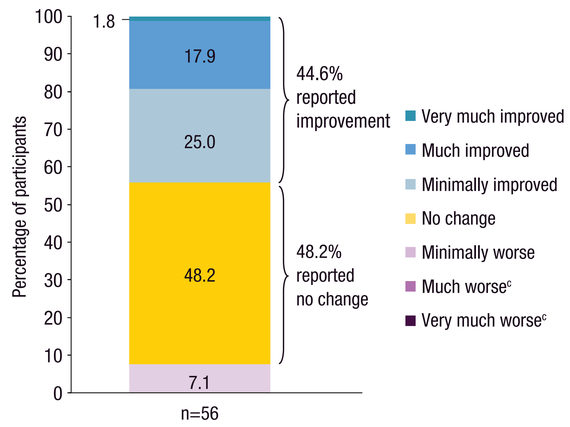
[a]Includes all enrolled participants who took ≥1 dose of sodium oxybate after providing informed consent.
Max, maximum; min, minimum; SD, standard deviation.

- Baseline demographics were similar to those reported in a prior real-world study of patients with narcolepsy taking SXB[12]

**Figure 2. Most Participants Reported Improvement or No Change in Narcolepsy Symptoms (PGIc), Reported That the Transition to LXB Was Easy (EOSMS), and Preferred LXB Over SXB (FPQ)[a,b]**

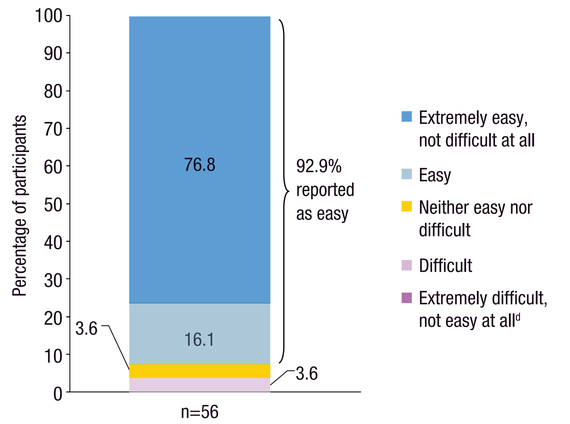
**Patient Global Impression of Change (PGIc)[c]**

Please choose the response below that best describes the overall change in your narcolepsy since you started taking the study medication (XYWAV)



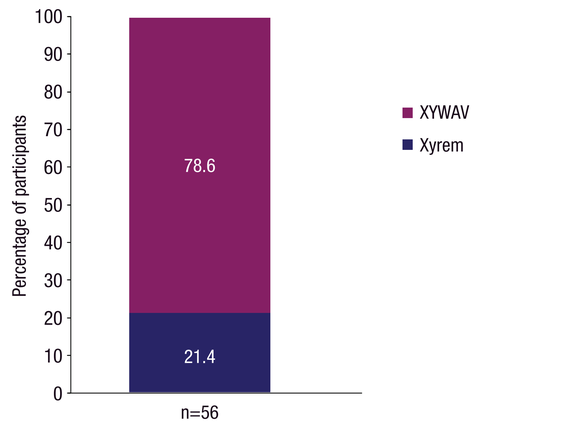

**Ease of switching medication scale (EOSMS)**

The process of switching to the new medication was:




**Forced preference questionnaire (FPQ)**

Thinking about your experience with Xyrem and XYWAV, which would you prefer to treat your narcolepsy?




[a]End of treatment or early discontinuation. [b]Includes participants with ≥1 PGIc, EOSMS, and FPQ assessment performed at the end of treatment or early discontinuation. [c]No participants reported that their symptoms were "much worse" or "very much worse" on the PGIc. [d]No participants reported that switching was "extremely difficult, not easy at all" on the EOSMS.
EOSMS, ease of switching medication scale; FPQ, forced preference questionnaire; LXB, low-sodium oxybate; PGIc, Patient Global Impression of Change; SXB, sodium oxybate.

**Table 4. Most Participants Remained on the Same Total Nightly Dose for the Duration of the Study and Continued Taking LXB Twice Nightly After Switching From SXB to LXB Gram-for-Gram**

| Parameter | SXB Baseline Period | LXB Start of Intervention Period | LXB End of Intervention Period[a] |
|---|---|---|---|
| **n** | 62 | 60 | 60[b] |
| **Total nightly dose, g/night[c]** | | | |
| Mean (SD) | 8.0 (1.4) | 8.0 (1.5) | 8.0 (1.4) |
| Median (min, max) | 8.8 (2.3, 9.0) | 8.5 (2.3, 9.0) | 9.0 (2.3, 9.0) |
| **Dosing regimen, n (%)** | | | |
| Once nightly | 2 (3.2) | 2 (3.3) | 2 (3.3) |
| Twice nightly | 58 (93.5) | 56 (93.3) | 56 (93.3) |
| Thrice nightly | 2 (3.2) | 2 (3.3) | 2 (3.3) |

[a]End of treatment or early discontinuation. [b]Includes 4 participants who did not achieve a stable LXB dose/regimen due to early termination from the study (2 participants because of protocol violations; 1 participant following an adverse event; 1 participant after withdrawal of consent). [c]Maximum allowed dose was 9 g/night.
LXB, low-sodium oxybate; max, maximum; min, minimum; SD, standard deviation; SXB, sodium oxybate.

**Table 5. The Majority of Participants Reported Only Mild to Moderate TEAEs During the Intervention (LXB) Period[a]**

| Category[b] | LXB Intervention Period |
|---|---|
| **n** | 60 |
| **Participants with ≥1 TEAE, n (%)** | 18 (30.0) |
| Mild | 11 (18.3) |
| Moderate | 5 (8.3) |
| Severe | 1 (1.7) |
| Life threatening | 1 (1.7) |
| **Participants with ≥1 TEAE related to study drug[c], n (%)** | 5 (8.3) |
| **Participants with ≥1 serious TEAE[d], n (%)** | 1 (1.7) |
| **Participants with ≥1 TEAE leading to discontinuation of study drug, n (%)** | 2 (3.3) |
| **Participants with ≥1 TEAE leading to dose reduction of study drug[e], n (%)** | 2 (3.3) |

[a]TEAEs that began or worsened after administration of the first LXB dose (not including the safety follow-up period). [b]Participants reporting >1 TEAE under a category are counted only once within that category. [c]Judged as related by the investigator; TEAEs with a missing relationship to study drug are classified as related. [d]One serious TEAE of hyperkalemia; this event was judged as not related to study drug by the investigator. In the phase 3 clinical trial of LXB in adults with narcolepsy, median changes from baseline in calcium, magnesium, potassium, and sodium were relatively minimal during the 16-week main study period, and no clinically meaningful trends were observed for electrolytes.[2] [e]One participant reduced the dose of LXB due to a treatment-related TEAE (sedation complication).
LXB, low-sodium oxybate; TEAE, treatment-emergent adverse event.

## Conclusions

- In this clinical study, patients with narcolepsy taking SXB switched from SXB to LXB with minimal modifications of dose/regimen, and reported that the transition process was easy
- Efficacy of oxybate treatment was maintained, and most participants preferred LXB over SXB
- Most TEAEs were mild to moderate after patients were switched to LXB

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**Disclosures: EB Leary** is a former full-time employee of Jazz Pharmaceuticals who, in the course of this employment, received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals, plc. **C Pfister, DS Fuller,** and **W Macfadden** are full-time employees of Jazz Pharmaceuticals who, in the course of this employment, have received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals, plc.

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