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Sleep Actigraphy in Participants With Narcolepsy or Idiopathic Hypersomnia Taking Low-Sodium Oxybate: Results From the DUET Study

DUET STUDY 407

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Introduction

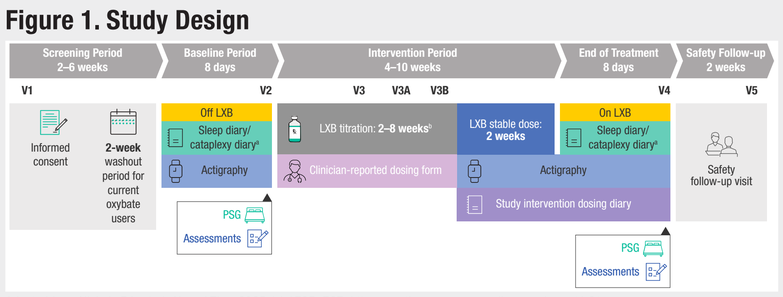
- Individuals with narcolepsy experience disrupted nighttime sleep,[1-3] and individuals with idiopathic hypersomnia often report nonrestorative nighttime sleep[4]
- Nocturnal sleep is typically assessed with polysomnography (PSG); however, it can be challenging to obtain recordings under conditions reflective of sleep behaviour at home, and consensus on a standard PSG protocol to capture excess sleep has not been established[5]
  - Actigraphy provides an empirical, noninvasive, longitudinal method for estimating sleep patterns in real-world settings, but there are limited actigraphy studies in individuals with central disorders of hypersomnolence[6-8]
- Low-sodium oxybate (LXB; Xywav®) is approved by the US Food and Drug Administration for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age or older with narcolepsy and the treatment of idiopathic hypersomnia in adults[9-12]
- Jazz DUET (**D**evelop hypersomnia **U**nderstanding by **E**valuating low-sodium oxybate **T**reatment) was a phase 4, prospective, open-label study (NCT05875974) to assess effectiveness of LXB on sleep and daytime symptoms in participants with narcolepsy (type 1 [NT1] or 2 [NT2]) or idiopathic hypersomnia

Objective

- To evaluate the effectiveness of LXB treatment on sleep parameters as assessed by actigraphy in individuals with narcolepsy or idiopathic hypersomnia

Methods

Figure 1. Study Design



Adapted from Nichols DA, et al. *Neurol Ther.* 2025;14:1705–727. http://creativecommons.org/licenses/by-nc/4.0/.
[a]Cataplexy diary in narcolepsy type 1 only. [b]Weekly titration visits were by teleconference. Visit 3 occurred on titration day 14. Titration could take between 2 and 8 weeks. Additional in-clinic visits were scheduled for day 35 (visit 3A) and day 56 (visit 3B), as needed. Investigator could optimise participant dosage and move to SDP at visit 3, 3A, or 3B, but not during intervening weekly teleconferences.
LXB, low-sodium oxybate; PSG, polysomnography; SDP, stable-dose period; V, visit.

- DUET included a screening period (with a washout period for oxybate users), a baseline (BL) period, a titration period (participants began LXB treatment with individualised dosing adjustments to achieve their optimal dose), a stable-dose period (SDP; at optimal LXB dose), an end-of-treatment (EOT) period, and a safety follow-up
  - **Narcolepsy cohort:** participants took LXB twice nightly (per US prescribing label; a maximum of 9 g/night for twice-nightly regimen, divided into 2 equal or unequal doses with the second dose taken 2.5–4 hours after the first dose)[9]
  - **Idiopathic hypersomnia cohort:** participants took a once- or twice-nightly LXB regimen based on the investigator's discretion (per US prescribing label; a maximum of 6 g/night for once-nightly or a maximum of 9 g/night for twice-nightly regimens, divided into 2 equal or unequal doses with the second dose taken 2.5–4 hours after the first dose)[9]
- Wrist actigraphy devices (GENEActiv; Activinsights; Cambridgeshire, UK) were used to estimate sleep parameters based on validated algorithms
  - Participants were instructed to wear the actigraphy device on the wrist of their nondominant hand during the BL, SDP, and EOT periods (analyses reported here included the 8 days leading up to the BL and EOT in-laboratory PSG visits)
  - The device was a waterproof, triaxial accelerometer that captured unfiltered, high-resolution raw data at a frequency set to 20 Hz, enabling continuous recording up to 30 days
  - Raw triaxial acceleration data were processed using R (v4.1.2), utilizing open-source GENEAread (v2.0.8)[13] and GENEAclassify (v1.5.3)[14] packages for data importation, calibration, and rest/activity classification
  - Autocalibration procedures were implemented to reduce sensor drift and calibration bias, enhancing data accuracy[15]
- Exploratory outcomes included actigraphy assessments of total nocturnal sleep time, number of nocturnal awakenings, sleep onset latency (SOL), and wake after sleep onset (WASO) at BL and EOT
  - Participants were required to have at least 5 of 8 days of actigraphy data in the BL and EOT periods to be included in analysis
- For all endpoints, the least squares (LS) mean differences (95% confidence interval [CI]) between EOT and BL were estimated using an analysis of covariance model adjusted for the BL value
  - *P* values were not adjusted for multiplicity
- The safety analysis set includes all participants who enrolled in the study and took their prescribed LXB regimen for ≥1 night after the BL period; the completer analysis set includes all participants who enrolled in the study, took their prescribed LXB regimen for ≥1 night after the BL period, completed the SDP, and completed the PSG EOT visit

Figure 2. Inclusion/Exclusion Criteria

Key Inclusion Criteria

- 18–75 years of age with primary diagnosis of NT1 or NT2 (per ICSD-3 or DSM-5) or primary diagnosis of idiopathic hypersomnia (per ICSD-3 criteria)
  - Individuals with and without long sleep time were included[a]
- ESS score >10[b]
- Participants were allowed to continue taking concomitant alerting agents (stimulants or wake-promoting agents), but had to have been taking the same dosage for ≥1 month before screening visit 1 with no plan to adjust dosage during the study period

Key Exclusion Criteria

- Untreated/inadequately treated sleep-disordered breathing (AHI >10)[c]
- History/presence of other untreated/inadequately treated sleep disorder or unstable/clinically significant medical condition, behavioural/psychiatric disorder, neurologic disorder, or surgical history that might affect the participant's safety or interfere with study conduct

[a]Analyses are performed for the complete idiopathic hypersomnia cohort, with no distinction made between those with and without long sleep time. [b]At screening visit 1 or at visit 2 if taking an oxybate medication at screening, after the washout period. [c]Hypopnoea definition included a ≥4% desaturation per Rule 1B *The AASM Manual for the Scoring of Sleep and Associated Events*,[16] as assessed during the baseline PSG visit.
AHI, apnoea-hypopnoea index; AASM, American Academy of Sleep Medicine; ESS, Epworth Sleepiness Scale; ICSD-3, *International Classification of Sleep Disorders – Third Edition*; NT1, narcolepsy type 1; NT2, narcolepsy type 2; PSG, polysomnography.

Results

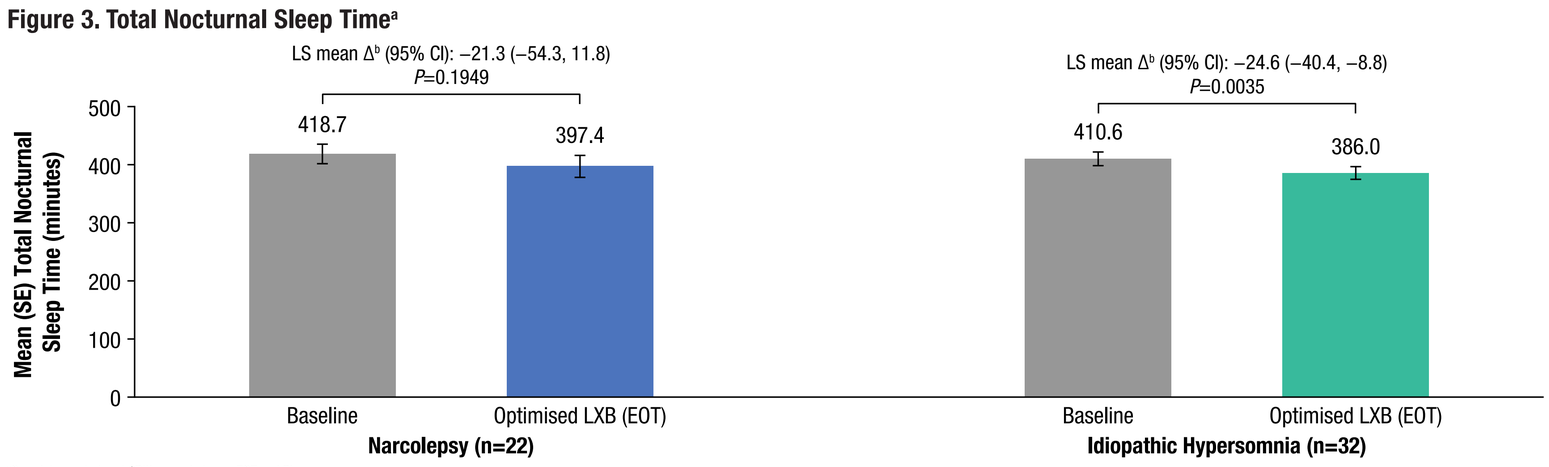
Table 1. Demographics and Baseline Characteristics[a]

Characteristic	Narcolepsy[a] (N=55)	Idiopathic Hypersomnia[a] (N=46)
Age (years), mean (SD)	33.4 (12.9)	38.1 (11.8)
Sex at birth, n (%)		
Male	15 (27.3)	9 (19.6)
Female	40 (72.7)	37 (80.4)
Race, n (%)		
White	44 (80.0)	39 (84.8)
Black or African American	7 (12.7)	3 (6.5)
American Indian or Alaska Native	0	0
Asian	2 (3.6)	2 (4.3)
Native Hawaiian or other Pacific Islander	0	1 (2.2)
Multiple[b]	1 (1.8)	1 (2.2)
Body mass index (kg/m²), mean (SD)	29.5 (6.7)	28.5 (6.4)
Oxybate type at study entry, n (%)		
Naive[c]	42 (76.4)	37 (80.4)
Low-sodium obybate	6 (10.9)	9 (19.6)
Sodium oxybate	5 (9.1)	0
Once-nightly sodium oxybate	2 (3.6)	0
Concomitant alerting agent, n (%)[d,e,f]	31 (56.4)	19 (41.3)

[a]Safety analysis set. [b]One (1.8%) participant with narcolepsy and 1 (2.2%) with idiopathic hypersomnia reported >1 race; race for 1 (1.8%) participant with narcolepsy was unknown. [c]No oxybate use within 2 weeks of entering the study. [d]Participants could have been taking multiple alerting medications. [e]Agents could have been prescribed for excessive sleepiness, idiopathic hypersomnia, and/or another condition. [f]Concomitant medications had a stop date on or after the date of the first dose of the study intervention or were ongoing.
SD, standard deviation.

- A total of 16 (47.1%) participants with NT1 and 18 (52.9%) participants with NT2 were included in the completer analysis set (13 participants in the narcolepsy cohort transferred to a different study cohort, results reported elsewhere)
- A total of 40 participants with idiopathic hypersomnia were included in the completer analysis set
- Twenty-two participants with narcolepsy (NT1, n=10; NT2, n=12) and 32 participants with idiopathic hypersomnia had evaluable actigraphy data at BL and EOT for at least 5 days in each period; missing data were due to device failures, insufficient wear time, and electronic capture/transfer errors

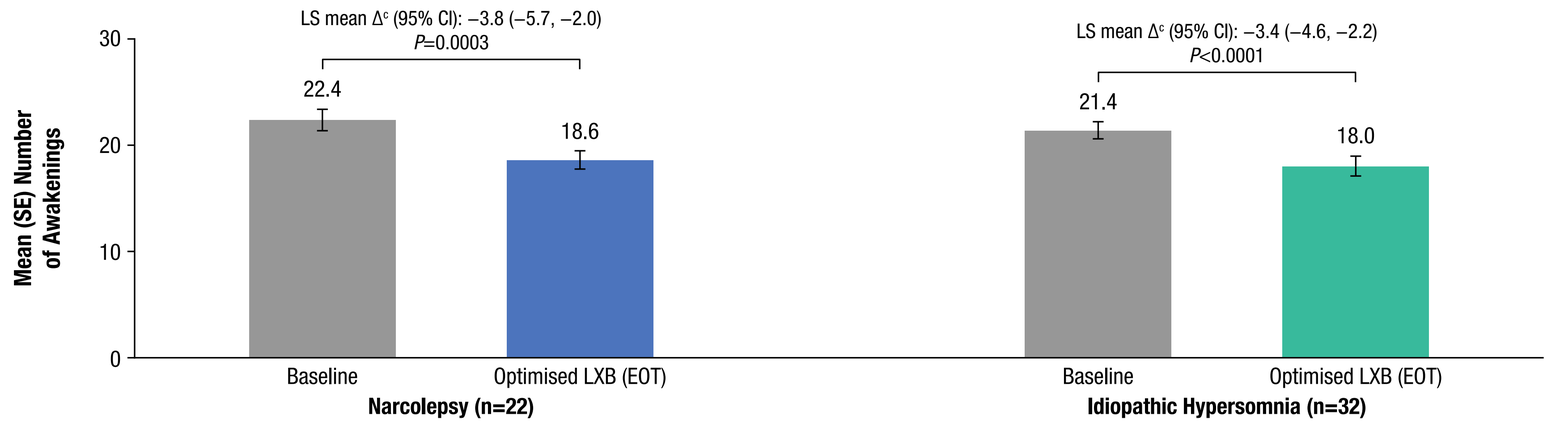
Figure 3. Total Nocturnal Sleep Time[a]



[a]Completer analysis set. [b]Difference between EOT and BL.
BL, baseline; CI, confidence interval; EOT, end of treatment; LS, least squares; LXB, low-sodium oxybate; SE, standard error.

- Mean total nocturnal sleep time numerically decreased from BL to EOT in participants with narcolepsy and decreased in participants with idiopathic hypersomnia

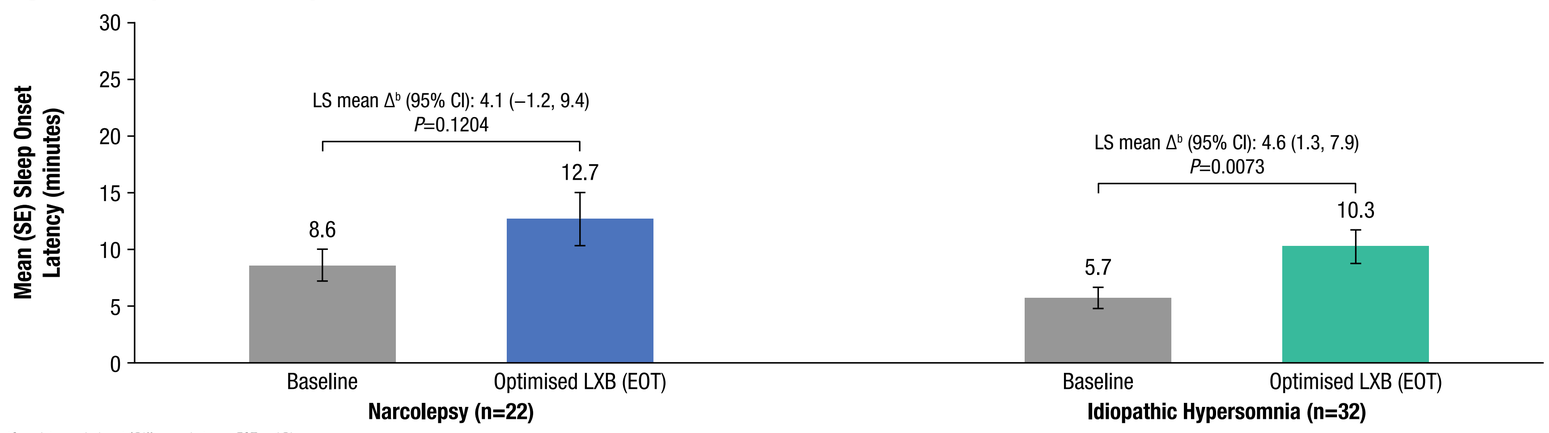
Figure 4. Number of Nocturnal Awakenings[a,b]



[a]Number of inactive and active events (>10 seconds length) of non-sleep taking place during the sleep interval. [b]Completer analysis set. [c]Difference between EOT and BL.
BL, baseline; CI, confidence interval; EOT, end of treatment; LS, least squares; LXB, low-sodium oxybate; SE, standard error.

- Mean number of nocturnal awakenings decreased from BL and EOT in participants with narcolepsy and in participants with idiopathic hypersomnia

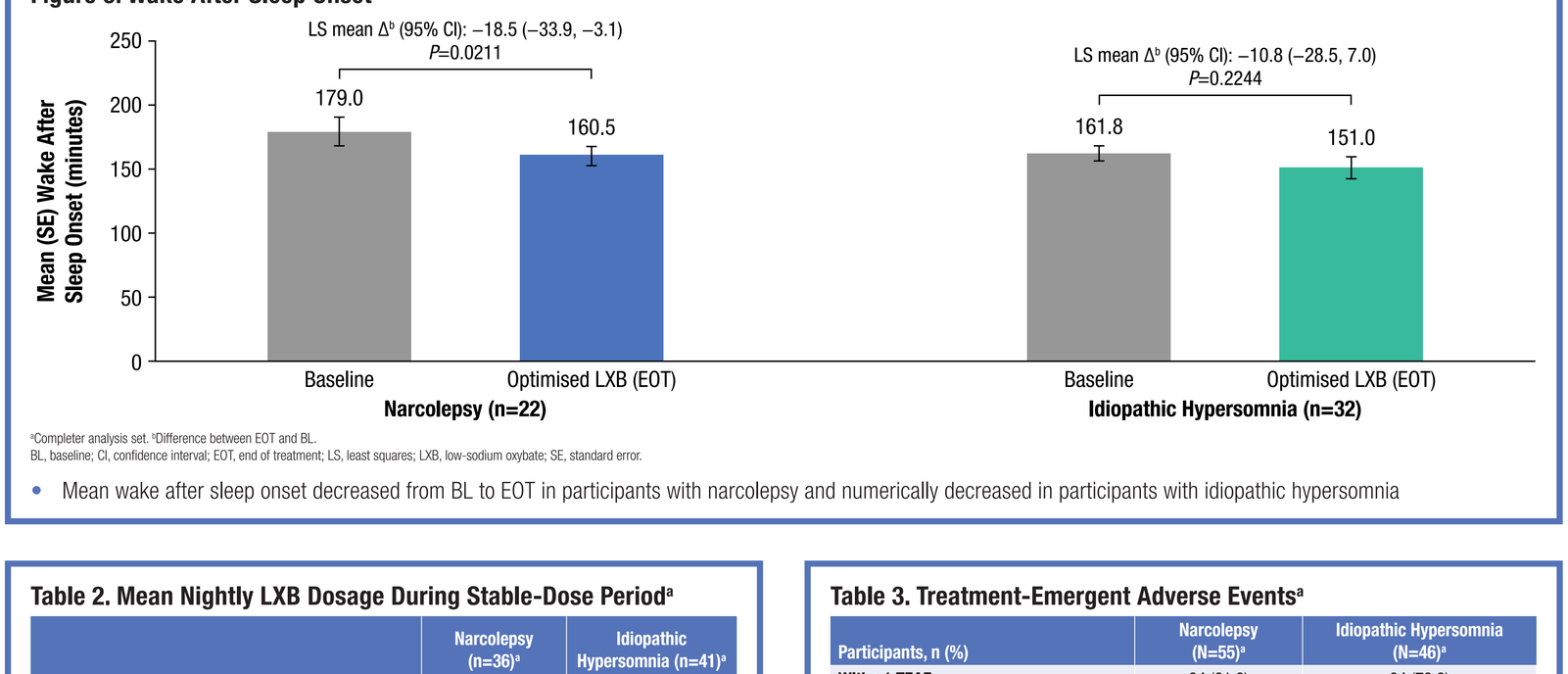
Figure 5. Sleep Onset Latency[a]



[a]Completer analysis set. [b]Difference between EOT and BL.
BL, baseline; CI, confidence interval; EOT, end of treatment; LS, least squares; LXB, low-sodium oxybate; SE, standard error.

- Mean sleep onset latency numerically increased from BL to EOT in participants with narcolepsy and increased in participants with idiopathic hypersomnia

Figure 6. Wake After Sleep Onset[a]



[a]Completer analysis set. [b]Difference between EOT and BL.
BL, baseline; CI, confidence interval; EOT, end of treatment; LS, least squares; LXB, low-sodium oxybate; SE, standard error.

- Mean wake after sleep onset decreased from BL to EOT in participants with narcolepsy and numerically decreased in participants with idiopathic hypersomnia

Table 2. Mean Nightly LXB Dosage During Stable-Dose Period[a]

	Narcolepsy (n=36)[a]	Idiopathic Hypersomnia (n=41)[a]
Total once-nightly dosage (g/night)		n=15
Mean (SD)	–	4.8 (1.1)
Total twice-nightly dosage (g/night)	n=36	n=26
Mean (SD)	7.0 (1.6)	7.7 (1.2)
First nightly LXB dose, mean (SD)	3.7 (0.9)	4.0 (0.8)
Second nightly LXB dose, mean (SD)	3.4 (0.9)	3.6 (0.8)

[a]Includes participants from the safety analysis set who reached the SDP. Once a participant reached an optimised dosage, they continued this dosage as a stable regimen during the SDP and EOT period.
BL, baseline; LXB, low-sodium oxybate; max, maximum; min, minimum; SD, standard deviation; SDP, stable-dose period.

- All participants with narcolepsy took twice-nightly LXB
- Fifteen (36.6%) participants with idiopathic hypersomnia took once-nightly LXB and 26 (63.4%) took twice-nightly LXB

Table 3. Treatment-Emergent Adverse Events[a]

Participants, n (%)	Narcolepsy (N=55)[a]	Idiopathic Hypersomnia (N=46)[a]
With ≥1 TEAE	34 (61.8)	34 (73.9)
With ≥1 TEAE related to treatment	30 (54.5)	30 (65.2)
TEAEs occurring in ≥10% of participants		
Nausea	13 (23.6)	9 (19.6)
Dizziness	8 (14.5)	8 (17.4)
Headache	7 (12.7)	8 (17.4)
Somnolence	6 (10.9)	3 (6.5)
Vomiting	6 (10.9)	5 (10.9)

[a]Safety analysis set.
TEAE, treatment-emergent adverse event.

- In the narcolepsy cohort, treatment-emergent adverse events (TEAEs) were mild or moderate in severity; no participants had a serious TEAE
- In the idiopathic hypersomnia cohort, TEAEs were mild or moderate in severity; 1 (2.2%) participant had a serious TEAE (hypoxia [concurrent with influenza] that was moderate in severity, determined to be unrelated to the study drug according to the investigator, and resolved)

Conclusions

- Based on actigraphy, participants with narcolepsy taking LXB showed fewer awakenings and decreased WASO compared with BL (off-LXB), suggesting less disrupted sleep with LXB treatment
- Participants with idiopathic hypersomnia taking LXB showed fewer awakenings compared with BL (off-LXB), suggesting improved sleep measures with LXB treatment, as well as decreased nocturnal sleep time
- These results augment previously reported PSG findings in these participants (see **Poster 184** and **Poster 120** for narcolepsy and idiopathic hypersomnia, respectively), adding to the established effectiveness of LXB treatment for narcolepsy and idiopathic hypersomnia

References: 1. Jimenez-Correa U, et al. *Arquivos de neuro-psiquiatria.* 2009;67:995-1000. **2.** Roth T, et al. *J Clin Sleep Med.* 2013;9:955-65. **3.** Maski K, et al. *J Clin Sleep Med.* 2022;18:289-304. **4.** Vernet C, et al. *J Sleep Res.* 2010;19:525-34. **5.** Fronczek R, et al. *Sleep.* 2020;43:zsaa044. **6.** Filardi M, et al. *Sleep Med.* 2015;16:126-30. **7.** Sadeh A. *Sleep Med Rev.* 2011;15:259-67. **8.** Cook JD, et al. *J Clin Sleep Med.* 2019;15:597-602. **9.** Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2023. **10.** Szarfman A, et al. *N Engl J Med.* 1995;333:1291. **11.** US Food and Drug Administration. Clinical review for Binosto, NDA 202344. 2012. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202344Orig1s000MedR.pdf. **12.** 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. **13.** Package GENEAread: Package for Reading Binary Files: CRAN; 2024 [August 25, 2025]. http://cran.r-project.org/web/packages/GENEAread/index.html **14.** Package GENEAclassify: Segmentation and Classification of Accelerometer Data: CRAN; 2024 [August 25, 2025]. http://cran.r-project.org/web/packages/GENEAclassify/index.html **15.** van Hees VT, et al. *J Appl Physiol.* 2014;117(7):738-44 **16.** Berry RB, et al. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications, Version 3. Darien, IL: American Academy of Sleep Medicine; 2023.

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