551

Narcolepsy Treatment Trends and Change in Alerting Agent Use After Low-Sodium Oxybate Initiation

Sarah C. Markt, ScD, MPH[1]; Marisa Whalen, PharmD[2]; Jessica K. Alexander, PhD[1]; Caroleen Drachenberg, PhD, MSPH[1]; Natalie Gavrielov, PhD[1]; Silky Beaty, PharmD, MSPH[2]; Elizabeth M. Poole, PhD[1]; John Kroner, MS[3]; Dionna Attinson, MPH[3]; Shaina Desai, MPH[3]; Jed Black, MD[1,4]; Michael J. Thorpy, MD[5]

[1]Jazz Pharmaceuticals, Palo Alto, CA, USA; [2]Jazz Pharmaceuticals, Philadelphia, PA, USA; [3]Aetion, Inc., New York, NY, USA; [4]Center for Sleep Sciences and Medicine, Stanford University School of Medicine, Palo Alto, CA, USA; [5]Albert Einstein College of Medicine, Bronx, NY, USA

Introduction

- Narcolepsy, a central disorder of hypersomnolence, comprises 2 subtypes (types 1 and 2) and is primarily characterized by excessive daytime sleepiness (EDS), disrupted nighttime sleep, and cataplexy (type 1)[1]
- Low-sodium oxybate (LXB; Xywav®) was US Food and Drug Administration (FDA)-approved in July 2020 to treat cataplexy or EDS in individuals aged ≥7 years with narcolepsy[2–5]
  - Sodium oxybate (SXB; Xyrem®) was FDA-approved to treat cataplexy (in 2002) and EDS (in 2005) among adults with narcolepsy (and among individuals aged ≥7 years in 2018)[6,7]
- Additional treatments used on- and off-label for narcolepsy include alerting agents (defined as stimulants and/or wake-promoting agents) and other treatments, such as antidepressants[8]
- **I**diopathic Hypersomnia and **N**arcolepsy **TRE**atment **P**atterns and Descriptive Ep**ID**emiology (INTREPID) is designed to understand real-world treatment patterns in individuals with idiopathic hypersomnia or narcolepsy
  - Results for individuals with idiopathic hypersomnia are reported separately in **Poster 552**

Objective

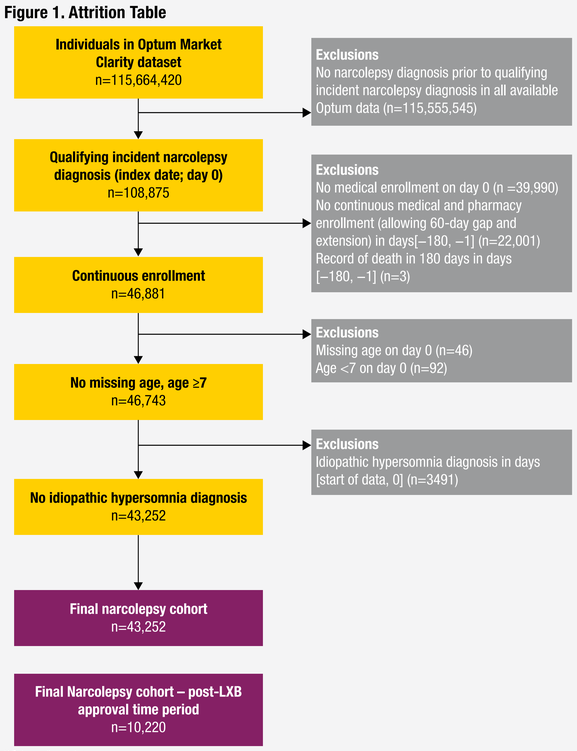
- To assess treatment patterns among individuals diagnosed with narcolepsy and evaluate changes in alerting agent claims following LXB initiation

Methods

- This retrospective cohort study used the Optum® Market Clarity™ linked electronic health records (EHR) and claims dataset to identify individuals with narcolepsy, aged ≥7 years, with ≥180 days medical/pharmacy enrollment prior to incident narcolepsy diagnosis (index date)
- Narcolepsy was defined as the occurrence of 2 medical claims for narcolepsy at least 1 day apart, using *International Classification of Diseases* (ICD-9 and ICD-10) codes
- Real-world treatment patterns were assessed following index until the end of the study period (July 1, 2007–September 30, 2023) and in the post-LXB approval period (July 22, 2020–September 30, 2023)
- Among individuals with claims for alerting agents prior to LXB initiation, reductions, discontinuations, switches, and no change in alerting agents were evaluated in the 180 days following LXB initiation
  - Reduction: a decrease in the average daily dose for an alerting agent or a reduction in the total number of unique alerting agents filled in the follow-up period, compared with the baseline period
  - Discontinuation: zero alerting agents filled in the follow-up period
  - Switch: the initiation of a new alerting agent in the follow-up period, compared with the baseline period, requiring that the total number of unique alerting agents filled remained the same across the baseline and follow-up periods
  - No change: no change in the alerting agent filled and no change in the average daily dose for an alerting agent filled in the follow-up period, compared with the baseline period

Results

Figure 1. Attrition Table



LXB, low-sodium oxybate.

- This study included 43,252 individuals diagnosed with narcolepsy, of whom 10,220 were diagnosed in the post-LXB approval period

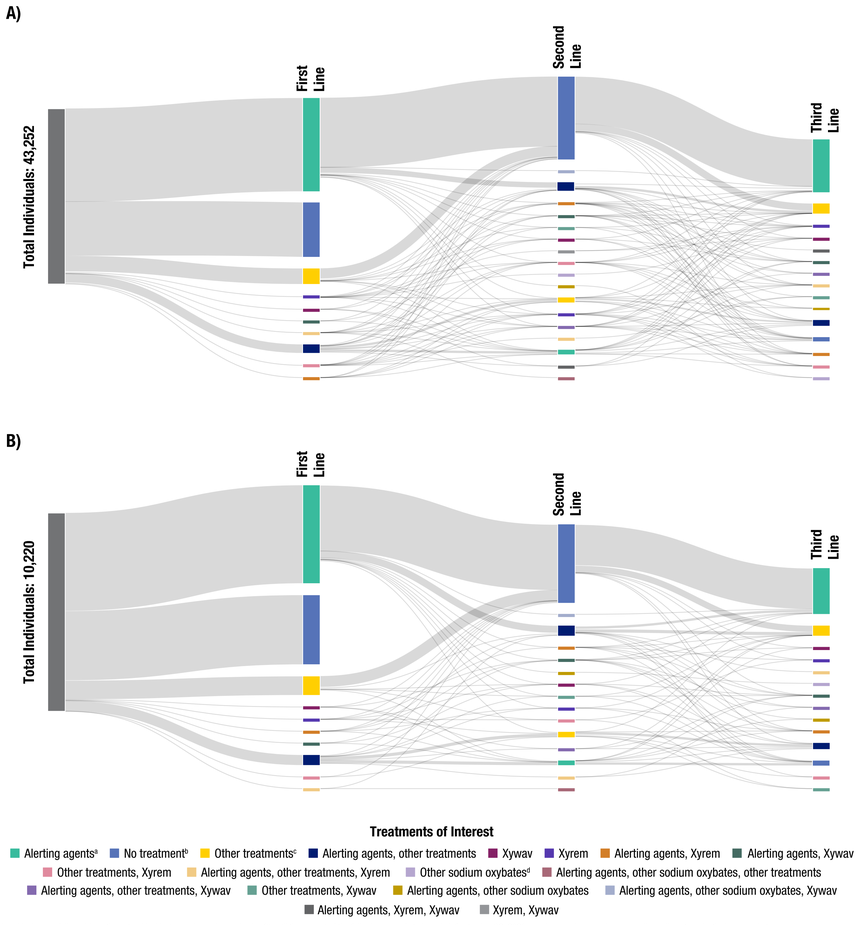
Table 1. Population Characteristics Among Individuals With Narcolepsy (2007–2023)

Characteristic	Individuals With Narcolepsy (n=43,252)
Mean (SD) age, years	42.8 (17.2)
Gender, n (%)	
Male	16,037 (37.1)
Female	27,206 (62.9)
Unknown	9 (0.0)
Race, n (%)	
White	31,123 (72.0)
Black	3936 (9.1)
Asian	499 (1.2)
Other/unknown	7694 (17.8)
Payer type, n (%)	
Commercial	27,360 (63.3)
Medicare	7082 (16.4)
Medicaid	7582 (17.5)
Other/unknown	1228 (2.8)
Select clinical characteristics,[a] n (%)	
Anxiety	13,034 (30.1)
Cardiovascular disease	6694 (15.5)
Depressive disorders	12,329 (28.5)
Diabetes or use of diabetes medication	9027 (20.9)
Headache/migraine	8554 (19.8)
Hyperlipidemia	10,555 (24.4)
Hypertension[b]	17,396 (40.2)
Obesity	8874 (20.5)
Other mood disorders	12,895 (29.8)
Sleep apnea	18,108 (41.9)

[a]Assessed in the 180 days prior to the incident narcolepsy diagnosis. [b]Defined as a hypertension diagnosis or antihypertensive prescription.
SD, standard deviation.

- The mean age of individuals with narcolepsy at diagnosis was 42.8 years; 62.9% were female, and the majority had narcolepsy type 2 (78.2%)
- The 3 most common comorbidities evaluated were sleep apnea (41.9%), hypertension (40.2%), and anxiety (30.1%)
- Additional demographic and clinical characteristics are presented in the supplemental material, available by scanning the QR code in the lower right corner of the poster

Figure 2. Treatment Patterns in the (A) Overall Follow-up Period (July 1, 2007–September 30, 2023) and (B) Post-LXB Approval Period (July 22, 2020–September 30, 2023)



Individuals were followed from the date of incident narcolepsy diagnosis (day 0) until the earliest of the following: end of study period (September 30, 2023), medical or pharmacy insurance disenrollment, or death. A comma between drug groups indicates individuals had claims for combination therapy (defined as an overlap of ≥30 days between prescriptions/claims).
[a]Alerting agents include stimulants (eg, amphetamine, methylphenidate) and wake-promoting agents (eg, modafinil, armodafinil, solriamfetol, pitolisant). [b]No treatment indicates a period of ≥31 days during which no prescription fill was identified. [c]The 5 most frequent other treatments were fluoxetine, venlafaxine, baclofen, atomoxetine, and clomipramine or imipramine. [d]Other sodium oxybates include fixed-dose sodium oxybate and authorized Xyrem generics.

- In the overall and post-LXB approval periods, 69.1% and 64.7% of individuals with narcolepsy, respectively, had at least 1 claim for a narcolepsy treatment of interest
- In the overall and post-LXB approval periods, the most frequent first-line treatments were alerting agents (overall: 52.9%; 76.5% among those who received any treatment; post-LXB approval: 49.3%; 76.1% among those who received any treatment)

Table 2. Changes in Alerting Agents in 180 Days Following LXB Initiation

Individuals With Narcolepsy Who Had Alerting Agent Claims Prior to LXB Initiation	Overall (n=788)	SXB Claim Prior to LXB Initiation (n=505)	No SXB Claim Prior to LXB Initiation (n=283)
Changes in alerting agent claims in the 180 days on and after LXB initiation,[a,b] n (%)			
Reduction	207 (26.3)	120 (23.8)	87 (30.7)
Discontinuation	131 (16.6)	73 (14.5)	58 (20.5)
Switch	42 (5.3)	17 (3.4)	25 (8.8)
No change	257 (32.6)	197 (39.0)	60 (21.2)

[a]Individuals were followed from the incident LXB prescription fill date (index date; day 0) until the earliest of the following: day 179 or LXB discontinuation (defined as the end date of the individual's last LXB fill). The baseline period was defined as the 180 days prior to the index date. [b]Values do not sum to 100% as some individuals may have increased their dosage or number of alerting agents.
LXB, low-sodium oxybate; SXB, sodium oxybate.

- Among 1032 individuals with narcolepsy who initiated LXB, 788 (76.4%) had at least 1 claim for alerting agents prior to LXB initiation
- Of these individuals, 42.9% experienced an alerting agent reduction or discontinuation, 5.3% switched to another alerting agent, and 32.6% had no alerting agent changes following LXB initiation
- Among those with prior SXB, 38.2% (n=193/505) experienced a reduction or discontinuation in alerting agents following LXB initiation; 51.2% of those without prior SXB experienced a reduction or discontinuation of alerting agents (n=145/283)

Table 3. Select Baseline Characteristics Among Alerting Agent Change Groups Following LXB Initiation

	Alerting Agent Reduction (n=207)	Alerting Agent Discontinuation (n=131)	Alerting Agent Switch (n=42)	No Change in Alerting Agents (n=257)
Mean (SD) age, years	36.4 (12.0)	37.4 (13.8)	31.8 (10.1)	40.6 (12.3)
Gender, n (%)				
Male	57 (27.5)	33 (25.2)	12 (28.6)	86 (33.5)
Female	150 (72.5)	98 (74.8)	30 (71.4)	170 (66.1)
Unknown	0	0	0	1 (0.4)
Race, n (%)				
White	153 (73.9)	93 (71.0)	30 (71.4)	190 (73.9)
Black	7 (3.4)	7 (5.3)	1 (2.4)	19 (7.4)
Asian	5 (2.4)	6 (4.6)	1 (2.4)	1 (0.4)
Other/Unknown	42 (20.3)	25 (19.1)	10 (23.8)	47 (18.3)
Payer type, n (%)				
Commercial	156 (75.4)	99 (75.6)	29 (69.0)	211 (82.1)
Medicare	8 (3.9)	14 (10.7)	1 (2.4)	15 (5.8)
Medicaid	43 (20.8)	17 (13.0)	12 (28.6)	29 (11.3)
Other/unknown	0	1 (0.8)	0	2 (0.8)
Select clinical characteristics,[a] n (%)				
Anxiety	95 (45.9)	53 (40.5)	21 (50.0)	79 (30.7)
Cardiovascular disease	19 (9.2)	17 (13.0)	2 (4.8)	15 (5.8)
Depressive disorders	75 (36.2)	39 (29.8)	14 (33.3)	59 (23.0)
Diabetes or use of diabetes medication	44 (21.3)	23 (17.6)	7 (16.7)	48 (18.7)
Headache/migraine	42 (20.3)	32 (24.4)	9 (21.4)	46 (17.9)
Hyperlipidemia	33 (15.9)	17 (13.0)	6 (14.3)	36 (14.0)
Hypertension[b]	89 (43.0)	54 (41.2)	16 (38.1)	97 (37.7)
Obesity	41 (19.8)	23 (17.6)	9 (21.4)	50 (19.5)
Other mood disorders	79 (38.2)	42 (32.1)	16 (38.1)	70 (27.2)
Sleep apnea	84 (40.6)	53 (40.5)	17 (40.5)	82 (31.9)

[a]Assessed in the 180 days prior to the incident narcolepsy diagnosis. [b]Defined as a hypertension diagnosis or antihypertensive prescription.
LXB, low-sodium oxybate; SD, standard deviation.

- Compared with individuals who had no change in alerting agents, those who reduced or discontinued alerting agents following LXB initiation had a higher prevalence of several comorbidities, including anxiety, cardiovascular disease, depressive disorders, other mood disorders, hypertension, and sleep apnea
- Additional demographic characteristics are presented in the supplemental material, available by scanning the QR code in the lower right corner of the poster

Conclusions

- Following diagnosis, approximately 50% of individuals with narcolepsy were first treated with alerting agents
- Nearly 43% of individuals with narcolepsy reduced or discontinued alerting agents following initiation of LXB, with a higher proportion of alerting agent reduction or discontinuation among individuals without prior claims for SXB than among those with prior SXB
- Limitations of this study include potential misclassification of diagnosis, the capture of medications of interest prescribed for other conditions, a lack of information on whether treatments were used as prescribed, and a small sample size
- Diverse real-world treatment trajectories following a diagnosis of narcolepsy indicate the difficulty and complexity in treating this condition

References: 1. American Academy of Sleep Medicine. *International Classification of Sleep Disorders – Third Edition, Text Revision.* Darien, IL: American Academy of Sleep Medicine; 2023. **2.** Xywav® (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. **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/regulatoryinformation/search-fda-guidance-documents/quantitative-labeling-sodium-potassium-and-phosphorus-human-over-counter-and-prescription-drug. **6.** Xyrem® (sodium oxybate) oral solution, CIII [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **7.** Junnarkar G, et al. *Expert Opin Drug Discov.* 2022;17:109-19. **8.** Nishino S, et al. *Sleep Med.* 2007;8(4):373-99.

Support and Acknowledgments: This study was sponsored by Jazz Pharmaceuticals. Under the direction of the authors, Peloton Advantage, LLC (an OPEN Health company) employees Aeja Jackson, PhD, MS, and Eleanor Bush, MA, provided medical writing support and an editor provided editorial support for this poster, which were funded by Jazz Pharmaceuticals.

Disclosures: SC Markt, M Whalen, JK Alexander, C Drachenberg, N Gavrielov, S Beaty, and **EM Poole** 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. **J Kroner, D Attinson,** and **S Desai** are full-time employees of Aetion, Inc., and hold stock options or equity in Aetion. **J Black** is a part-time employee of Jazz Pharmaceuticals and shareholder of Jazz Pharmaceuticals, plc. **MJ Thorpy** has received research/grant support and consultancy fees from Axsome, Balance Therapeutics, Eisai Pharmaceuticals, Flamel/Avadel, Harmony Biosciences, Idorsia Pharmaceuticals, Jazz Pharmaceuticals, NLS Pharmaceuticals, Suven Life Sciences, Takeda Pharmaceutical, and XWPharma.

Scan this code to access this poster and supplemental material online.
This code is not for promotional purposes.

Presented at SLEEP 2025, the 39th Annual Meeting of the Associated Professional Sleep Societies, LLC (APSS); June 8–11, 2025; Seattle, WA, USA

551

Narcolepsy Treatment Trends and Change in Alerting Agent Use After Low-Sodium Oxybate Initiation

Sarah C. Markt, ScD, MPH[1]; Marisa Whalen, PharmD[2]; Jessica K. Alexander, PhD[1]; Caroleen Drachenberg, PhD, MSPH[1]; Natalie Gavrielov, PhD[1]; Silky Beaty, PharmD, MSPH[2]; Elizabeth M. Poole, PhD[1]; John Kroner, MS[3]; Dionna Attinson, MPH[3]; Shaina Desai, MPH[3]; Jed Black, MD[1,4]; Michael J. Thorpy, MD[5]

[1]Jazz Pharmaceuticals, Palo Alto, CA, USA; [2]Jazz Pharmaceuticals, Philadelphia, PA, USA; [3]Aetion, Inc., New York, NY, USA; [4]Center for Sleep Sciences and Medicine, Stanford University School of Medicine, Palo Alto, CA, USA; [5]Albert Einstein College of Medicine, Bronx, NY, USA

Supplemental Table 1. Additional Population Characteristics Among Individuals With Narcolepsy (2007–2023)

Characteristic	Individuals With Narcolepsy (n=43,252)
Ethnicity, n (%)	
Hispanic	1269 (2.9)
Not Hispanic	31,714 (73.3)
Unknown	10,269 (23.7)
US geographic region, n (%)	
Northeast	7184 (16.6)
South	11,228 (26.0)
Midwest	18,473 (42.7)
West	3841 (8.9)
Other/unknown	2526 (5.8)
Narcolepsy diagnosis type[a], n (%)	
Type 1	5601 (12.9)
Type 2	33,822 (78.2)
Both type 1 and type 2	3829 (8.9)
Sleep tests and services[b], n (%)	
CPAP	5897 (13.6)
Polysomnography	11,176 (25.8)
Multiple sleep latency test	5137 (11.9)
Home sleep test	641 (1.5)
Actigraphy test	112 (0.3)
Other sleep disorder test[c]	1759 (4.1)

[a]For individuals categorized as "Both type 1 and type 2", ICD-9 or ICD-10 diagnosis codes for both "narcolepsy type 1" and "narcolepsy type 2" were observed on or prior to the index date. [b]Assessed in the 180 days prior to the incident narcolepsy diagnosis. [c]Other sleep tests were identified among EHR encounters with any of the following HCPCS/CPT procedure codes: 95800, 95801, 95806, 95807.
CPAP, continuous positive airway pressure; CPT, Current Procedural Terminology; EHR, electronic health record; HCPCS, Healthcare Common Procedure Coding System; ICD-9, *International Classification of Diseases*, 9th Revision; ICD-10, *International Classification of Diseases*, 10th Revision; US, United States.

Supplemental Table 2. Additional Baseline Characteristics Among Alerting Agent Change Groups Following LXB Initiation

Characteristic	Alerting Agent Reduction (n=207)	Alerting Agent Discontinuation (n=131)	Alerting Agent Switch (n=42)	No Change in Alerting Agents (n=257)
Ethnicity, n (%)				
Hispanic	3 (1.4)	3 (2.3)	0	6 (2.3)
Not Hispanic	147 (71.0)	91 (69.5)	22 (52.4)	200 (77.8)
Unknown	57 (27.5)	37 (28.2)	20 (47.6)	51 (19.8)
US geographic region, n (%)				
Northeast	38 (18.4)	16 (12.2)	7 (16.7)	40 (15.6)
South	59 (28.5)	39 (29.8)	15 (35.7)	87 (33.9)
Midwest	78 (37.7)	54 (41.2)	14 (33.3)	82 (31.9)
West	21 (10.1)	12 (9.2)	1 (2.4)	26 (10.1)
Other/unknown	11 (5.3)	10 (7.6)	5 (11.9)	22 (8.6)
Sleep tests and services[a], n (%)				
CPAP	28 (13.5)	14 (10.7)	8 (19.0)	39 (15.2)
Polysomnography	34 (16.4)	23 (17.6)	10 (23.8)	20 (7.8)
Multiple sleep latency test	33 (15.9)	20 (15.3)	11 (26.2)	17 (6.6)
Home sleep test	2 (1.0)	0 (0.0)	2 (4.8)	3 (1.2)
Other sleep disorder test[b]	4 (1.9)	2 (1.5)	4 (9.5)	3 (1.2)

[a]Assessed in the 180 days prior to the incident narcolepsy diagnosis. [b]Other sleep tests were identified among EHR encounters with any of the following HCPCS/CPT procedure codes: 95800, 95801, 95806, 95807.
CPAP, continuous positive airway pressure; CPT, Current Procedural Terminology; EHR, electronic health record; HCPCS, Healthcare Common Procedure; LXB, low-sodium oxybate; US, United States.