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

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Introduction

- Idiopathic hypersomnia is a multi-symptom neurologic sleep disorder characterized by excessive daytime sleepiness; long, nonrestorative sleep; and severe sleep inertia[1]
- While low-sodium oxybate (LXB; Xywav®) is the only Food and Drug Administration-approved treatment for idiopathic hypersomnia[2–5] (August 12, 2021), individuals with idiopathic hypersomnia are often treated with medications prescribed off-label, such as alerting agents (defined as stimulants and/or wake-promoting agents), high-sodium oxybates, or treatments such as clarithromycin or flumazenil[6]
- **I**diopathic Hypersomnia and **N**arcolepsy **TRE**atment **P**atterns and Descriptive Ep**ID**emiology (INTREPID) is a study designed to understand real-world treatment patterns in patients with idiopathic hypersomnia or narcolepsy
  - Results for individuals with narcolepsy are reported separately in **Poster 551**

Objective

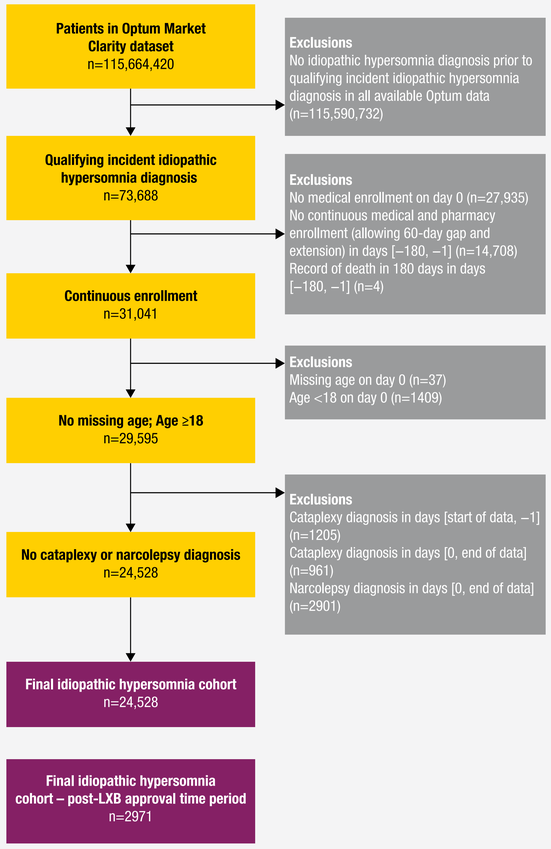
- To assess treatment patterns among individuals diagnosed with idiopathic hypersomnia and evaluate changes in alerting agent claims following LXB initiation

Methods

- This retrospective cohort study used the Optum® Market Clarity™ linked electronic health record (EHR) and claims dataset to identify individuals diagnosed with idiopathic hypersomnia, aged ≥18 years, with ≥180 days medical/pharmacy enrollment prior to incident idiopathic hypersomnia diagnosis (index date)
  - Idiopathic hypersomnia was defined as the first occurrence of a medical claim for idiopathic hypersomnia, using *International Classification of Diseases* (ICD-9 and ICD-10) codes
- 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 (August 12, 2021–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 to 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 period
  - 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 24,528 individuals diagnosed with idiopathic hypersomnia, of whom 2971 were diagnosed in the post-LXB approval period

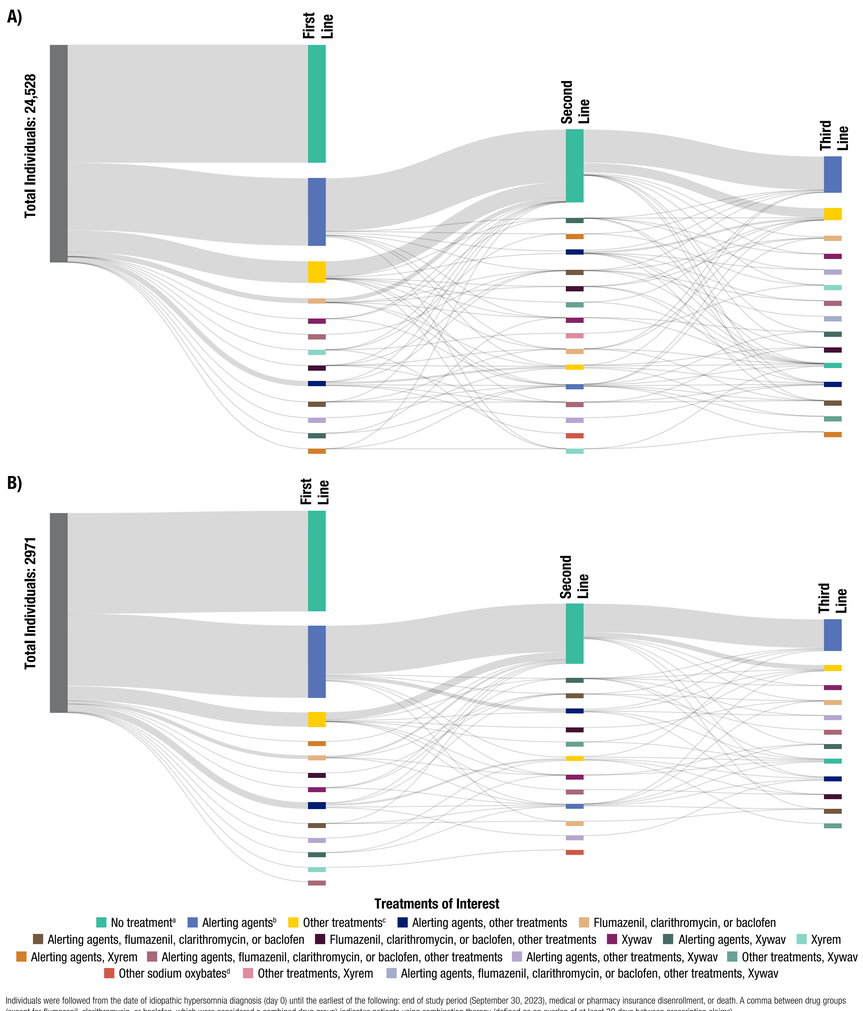
Table 1. Population Characteristics Among Individuals With Idiopathic Hypersomnia (2007–2023)

Characteristic	Individuals with Idiopathic Hypersomnia (n=24,528)
Mean (SD) age, years	45.8 (15.7)
Gender, n (%)	
Male	9397 (38.3)
Female	15,128 (61.7)
Unknown	3 (0.0)
Race, n (%)	
White	18,060 (73.6)
Black	1701 (6.9)
Asian	291 (1.2)
Other/unknown	4476 (18.2)
Payer type, n (%)	
Commercial	16,555 (67.5)
Medicare	3775 (15.4)
Medicaid	3602 (14.7)
Other/unknown	596 (2.4)
Select clinical characteristics[a], n (%)	
Anxiety disorders	6673 (27.2)
Cardiovascular disease	3906 (15.9)
Depressive disorders	6124 (25.0)
Diabetes or use of diabetes medication	5641 (23.0)
Headache/migraine	4423 (18.0)
Hyperlipidemia	7108 (29.0)
Hypertension[b]	10,641 (43.4)
Obesity	5811 (23.7)
Other mood disorders	6257 (25.5)
Sleep apnea	10,438 (42.6)

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

- The mean age at diagnosis was 45.8 years; 61.7% were female, and 73.6% were White
- The 3 most common comorbidities evaluated were hypertension (43.4%), sleep apnea (42.6%), and hyperlipidemia (29.0%)
- Additional baseline characteristics are presented in the supplemental material, available through 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 (August 12, 2021–September 30, 2023)



Individuals were followed from the date of idiopathic hypersomnia 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 (except for flumazenil, clarithromycin, or baclofen, which were considered a combined drug group) indicates patients using combination therapy (defined as an overlap of at least 30 days between prescription claims).
[a]"No treatment" indicates a period of at least 31 days during which no prescription fill was identified.
[b]Alerting agents include stimulants (eg, amphetamine, methylphenidate) and wake-promoting agents (eg, modafinil, armodafinil, solriamfetol, pitolisant).
[c]The 5 most frequent other treatments were fluoxetine, venlafaxine, atomoxetine, imipramine, and clomipramine.
[d]Other sodium oxybates include fixed-dose sodium oxybate and authorized Xyrem generics.
IH, idiopathic hypersomnia; LXB, low-sodium oxybate.

- Over a median of 2.3 years of follow-up, 45.9% had at least 1 claim for a predefined treatment of interest for idiopathic hypersomnia
- The most frequent first-line treatments were alerting agents (31.2% overall; 67.9% among those treated)
- During the post-LXB approval period (n=2971), 49.7% had at least 1 claim for an idiopathic hypersomnia treatment; the most common first-line treatments were alerting agents (36.2% overall; 72.9% among those treated)
- Among those treated in the second line in the post-LXB approval period, 19.8% were treated with alerting agents and 7.9% with alerting agents and LXB

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

Individuals With Idiopathic Hypersomnia Who Had Alerting Agent Claims Prior to LXB Initiation	Overall (n=96)	Idiopathic Hypersomnia With Long Sleep Time (n=74)	Idiopathic Hypersomnia Without Long Sleep Time (n=22)
Changes in alerting agent claims in the 180 days on and after LXB initiation,[a,b] n (%)			
Reduction	36 (37.5)	29 (39.2)	7 (31.8)
Discontinuation	15 (15.6)	14 (18.9)	1 (4.5)
Switch	8 (8.3)	8 (10.8)	0
No change	21 (21.9)	15 (20.3)	6 (27.3)

[a]Patients 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 patient'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.

- Among the 120 individuals who initiated LXB, 96 (80.0%) had claims for an alerting agent prior to LXB initiation
- Among those 96 individuals, 53.1% discontinued or reduced alerting agents, 8.3% switched, and 21.9% had no alerting agent changes following LXB initiation

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

	Alerting Agent Reduction (n=36)	Alerting Agent Discontinuation (n=15)	Alerting Agent Switch (n=8)	No Change in Alerting Agents (n=21)
Mean (SD) age, years	39.4 (12.3)	34.7 (9.2)	31.6 (9.4)	37.3 (11.6)
Gender, n (%)				
Male	8 (22.2)	2 (13.3)	3 (37.5)	4 (19.0)
Female	28 (77.8)	13 (86.7)	5 (62.5)	17 (81.0)
Race, n (%)				
White	28 (77.8)	10 (66.7)	4 (50.0)	20 (95.2)
Black	2 (5.6)	0	0	1 (4.8)
Asian	0	1 (6.7)	0	0
Other/unknown	6 (16.7)	4 (26.7)	4 (50.0)	0
Payer type, n (%)				
Commercial	30 (83.3)	13 (86.7)	7 (87.5)	17 (81.0)
Medicare	0	0	0	1 (4.8)
Medicaid	6 (16.7)	2 (13.3)	1 (12.5)	3 (14.3)
Select clinical characteristics,[a] n (%)				
Anxiety	17 (47.2)	5 (33.3)	4 (50.0)	7 (33.3)
Cardiovascular disease	4 (11.1)	0	0	1 (4.8)
Depressive disorders	17 (47.2)	7 (46.7)	4 (50.0)	8 (38.1)
Diabetes or use of diabetes medication	9 (25.0)	1 (6.7)	0	2 (9.5)
Headache/migraine	12 (33.3)	1 (6.7)	3 (37.5)	6 (28.6)
Hyperlipidemia	10 (27.8)	2 (13.3)	2 (25.0)	2 (9.5)
Hypertension[b]	16 (44.4)	2 (13.3)	3 (37.5)	8 (38.1)
Obesity	4 (11.1)	3 (20.0)	1 (12.5)	2 (9.5)
Other mood disorders	17 (47.2)	7 (46.7)	4 (50.0)	6 (28.6)
Sleep apnea	19 (52.8)	6 (40.0)	4 (50.0)	7 (33.3)

[a]Assessed in the 180 days prior to the incident idiopathic hypersomnia 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 after LXB initiation, those who reduced or discontinued alerting agents had a higher prevalence of several comorbidities, including depressive disorders, other mood disorders, hyperlipidemia, and sleep apnea
- Additional baseline characteristics among alerting agent change groups are presented in the supplemental material, available through the QR code in the lower right corner of the poster

Conclusions

- Treatment patterns showed numerous combinations of treatments and treatment trajectories following a diagnosis of idiopathic hypersomnia, highlighting the known difficulty and complexity in treating this condition
  - Many patients did not receive any treatment over the follow-up period, highlighting a significant treatment gap
- Limitations of this study include potential misclassification of the 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
- Alerting agent use was common prior to LXB initiation in individuals with idiopathic hypersomnia, and approximately 50% of these individuals discontinued or reduced alerting agents following LXB initiation

References: 1. Trotti LM. *Sleep Med Clin.* 2017;12(3):331-344. **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.** Saini P, Rye DB. *Sleep Med Clin.* 2017;12(1):47-60.

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

Individuals With Idiopathic Hypersomnia	n=24,528
Ethnicity, n (%)	
Hispanic	755 (3.1)
Not Hispanic	18,047 (73.6)
Unknown	5726 (23.3)
US geographic region, n (%)	
Northeast	3607 (14.7)
South	6354 (25.9)
Midwest	10,792 (44.0)
West	2437 (9.9)
Other/Unknown	1338 (5.5)
Idiopathic hypersomnia type[a], n (%)	
With long sleep time	16,399 (66.9)
Without long sleep time	8065 (32.9)
Both with long sleep time and without long sleep time	64 (0.3)
Sleep tests and services[b], n (%)	
Use of CPAP machine	3306 (13.5)
Polysomnography	5189 (21.2)
Multiple sleep latency test	2720 (11.1)
Home sleep test	466 (1.9)
Actigraphy test	65 (0.3)
Other sleep disorder test[c]	1270 (5.2)

[a]Idiopathic hypersomnia diagnosis type was categorized based on the ICD-9 or ICD-10 diagnosis codes observed on the index date. For patients categorized as "Both with long sleep time and without long sleep time", ICD-9 or ICD-10 diagnosis codes for both "idiopathic hypersomnia with long sleep time" and "idiopathic hypersomnia without long sleep time" were observed on the index date.
[b]Assessed in the 180 days prior to the incident idiopathic hypersomnia 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

	Alerting Agent Reduction (n=36)	Alerting Agent Discontinuation (n=15)	Alerting Agent Switch (n=8)	No Change in Alerting Agents (n=21)
Ethnicity, n (%)				
Hispanic	1 (2.8)	1 (6.7)	1 (12.5)	0
Not Hispanic	28 (77.8)	9 (60.0)	4 (50.0)	18 (85.7)
Unknown	7 (19.4)	5 (33.3)	3 (37.5)	3 (14.3)
US geographic region, n (%)				
Northeast	4 (11.1)	1 (6.7)	1 (12.5)	3 (14.3)
South	11 (30.6)	6 (40.0)	1 (12.5)	5 (23.8)
Midwest	14 (38.9)	6 (40.0)	3 (37.5)	10 (47.6)
West	7 (19.4)	0	1 (12.5)	3 (14.3)
Other/Unknown	0	2 (13.3)	2 (25.0)	0
Sleep tests and services[a], n (%)				
Use of CPAP machine	7 (19.4)	4 (26.7)	2 (25.0)	2 (9.5)
Polysomnography	12 (33.3)	5 (33.3)	4 (50.0)	3 (14.3)
Multiple sleep latency test	11 (30.6)	5 (33.3)	4 (50.0)	3 (14.3)
Home sleep test	1 (2.8)	1 (6.7)	0	0
Other sleep disorder test[b]	2 (5.6)	1 (6.7)	0	1 (4.8)

[a]Assessed in the 180 days prior to the incident idiopathic hypersomnia 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 Coding System; US, United States.