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Real-world Treatment Utilisation of Sodium Oxybate in Paediatric Patients With Narcolepsy: An Analysis of Claims Data

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Background

- Narcolepsy is a rare, lifelong, neurological disorder characterised by excessive daytime sleepiness and dysregulation of the sleep-wake cycle, including cataplexy, hypnagogic hallucinations, and sleep paralysis, though not all patients experience all symptoms[1]
- Sodium oxybate (SXB) is considered a standard of care for the treatment of narcolepsy[2]
- In paediatric narcolepsy clinical trials, median SXB compliance rates were very high, ranging from 83% to 100% for up to 47 weeks[3,4]
  - However, real-world SXB utilisation in paediatric patients has not been well studied

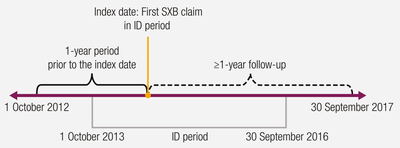
Objective

- To examine SXB adherence, persistence, and overall treatment utilisation patterns in real-world settings in paediatric patients with narcolepsy in the United States

Methods

- This retrospective cohort study identified US patients <18 years of age diagnosed with narcolepsy using de-identified commercial insurance claims from the Truven Health Analytics MarketScan® Commercial Claims and Encounters database from October 2012 through September 2017
- Patients with narcolepsy were first identified based on having ≥1 of the following: ≥1 nondiagnostic claim with a code for narcolepsy with or without cataplexy and ≥1 claim for SXB; ≥2 claims with a code for narcolepsy (1 being nondiagnostic); or ≥1 nondiagnostic claim with a code for narcolepsy following a Multiple Sleep Latency Test (MSLT)
  - Nondiagnostic claims were defined as claims for evaluation and management services without MSLT/polysomnography or other diagnostic testing
- For the analysis of SXB treatment patterns, narcolepsy patients who were being treated with ≥1 claim for SXB during the identification (ID) period (1 October 2013-30 September 2016) were identified
  - The first claim for SXB during the ID period was defined as the index date
  - Patients were required to have continuous enrolment for ≥1 year prior to and ≥1 year after the index date, with ≥1 nondiagnostic claim prior to the index date
  - New users were defined as those who did not have any SXB claims during the 1-year period prior to the index date; continuing users were defined as those who had ≥1 SXB claim during the 1-year period prior to the index date

Figure 1. Study Timeline for New Versus Continuing SXB Users



SXB, sodium oxybate; ID, identification.

- Treatment utilisation, adherence, and persistence of SXB were measured at 3 months, 6 months, 9 months, 1 year, and 2 years
  - Adherence was assessed as mean proportion of days covered (PDC) and proportion of patients with PDC ≥80%, and persistence was evaluated by mean number of days on continuous treatment (defined as treatment with an interruption of <60 days)
- Descriptive statistics were reported, and chi-square or *t* tests were performed to compare between-group treatment patterns. Kaplan-Meier curves were produced, and log-rank tests were performed to compare continuous time on treatment. *P* values were not controlled for multiplicity and, hence, are nominal
- Graphical analyses were performed to examine overall treatment patterns among adults with narcolepsy treated with any narcolepsy-related treatments (both indicated medications and those used to treat common comorbid conditions in patients with narcolepsy), including SXB, wake-promoting agents (WPAs), attention-deficit/hyperactivity disorder (ADHD) agents and traditional central nervous system (CNS) stimulants, antidepressants, and nonstimulant ADHD agents
  - The first claim for any narcolepsy-related treatment was considered the index date, with similar continuous enrolment requirements as described above
  - Patients were stratified as treatment-naïve (no treatment prior to index), newly treated with index treatment (no index treatment/treatment combination prior to index but who were not treatment-naïve), or continued index treatment (index treatment/treatment combination prior to index)

Results

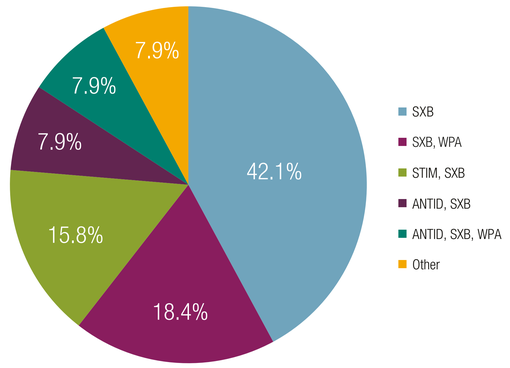
Table 1. Demographics of Paediatric Narcolepsy Patients Treated With SXB

Characteristic	All (n = 61)	New users (n = 38)	Continuing users (n = 23)	*P* value
Age, years, mean (SD)	14.6 (2.4)	14.9 (2.1)	14.0 (2.9)	0.193
Age group 12-17 years, n (%)	53 (86.9)	35 (92.1)	18 (78.3)	0.120
Female, n (%)	31 (50.8)	19 (50.0)	12 (52.2)	0.869
Geographic region, n (%)				0.671
Midwest	4 (6.6)	2 (5.3)	2 (8.7)	
Northeast	16 (26.2)	9 (23.7)	7 (30.4)	
South	30 (49.2)	21 (55.3)	9 (39.1)	
West	11 (18.0)	6 (15.8)	5 (21.7)	
Insurance type, n (%)				0.337
EPO	1 (1.6)	0	1 (4.3)	
HMO	5 (8.2)	3 (7.9)	2 (8.7)	
POS	2 (3.3)	2 (5.3)	0	
PPO	41 (67.2)	23 (60.5)	18 (78.3)	
POS with capitation	1 (1.6)	1 (2.6)	0	
CDHP	7 (11.5)	5 (13.2)	2 (8.7)	
HDHP	4 (6.6)	4 (10.5)	0	

SXB, sodium oxybate; SD, standard deviation; EPO, exclusive provider organisation; HMO, health maintenance organisation; POS, point of service; PPO, preferred provider organisation; CDHP, consumer-directed health plan; HDHP, high-deductible health plan.

- Among 61 continuously enrolled paediatric patients taking SXB (mean [±standard deviation] age, 14.6 [±2.4] years; 50.8% female), 38 were new SXB users and 23 were continuing SXB users

Figure 2. Initial Treatment Regimen[a,b] of Paediatric Narcolepsy Patients Newly Treated With SXB (n = 38)



'Other' included:	Percentage
ADHD, STIM, ANTID, SXB	2.6
STIM, ANTID, SXB, WPA	2.6
STIM, SXB, WPA	2.6

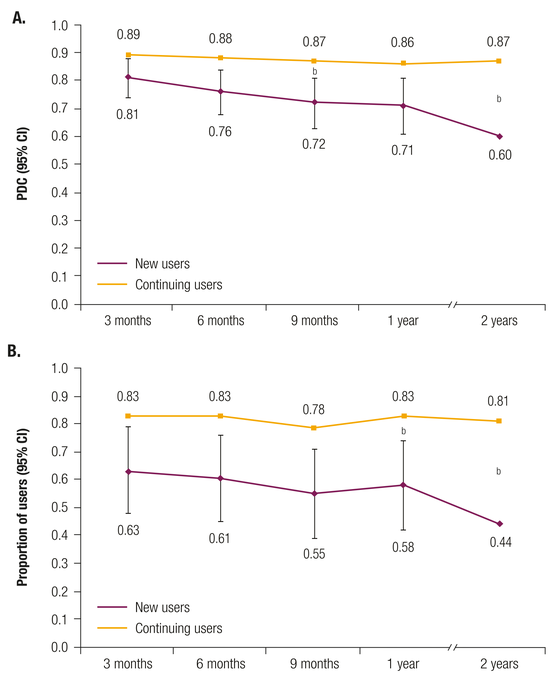
SXB, sodium oxybate; WPA, wake-promoting agent; ANTID, antidepressant; ADHD, attention-deficit/hyperactivity disorder; STIM, stimulant; CNS, central nervous system.

[a]Defined as all treatment classes occurring between the index date and 45 days after the index date.

[b]Regarding treatment classes, ADHD represents nonstimulant ADHD agents, while STIM represents traditional CNS stimulants (eg, amphetamine, methylphenidate).

- Among 38 new users, 42.1% (n = 16) received monotherapy and 57.9% (n = 22) received combination therapy
- Of new users receiving combination therapy (n = 22), 31.8% (n = 7) received SXB plus a WPA, 27.3% (n = 6) received SXB plus a traditional CNS stimulant, and 13.6% (n = 3) received SXB plus an antidepressant

Figure 3. (A) Mean PDC for New and Continuing SXB Users and (B) Proportion of New and Continuing SXB Users With PDC ≥80%[a]



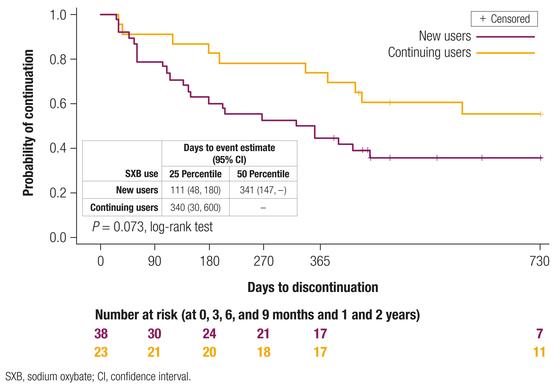
PDC, proportion of days covered; SXB, sodium oxybate; CI, confidence interval.

[a]95% CI values are not available where the sample size was <30.

[b]*P* <0.05.

- Measured by PDC and proportion of users with PDC ≥80%, adherence decreased over time for new users; however, adherence remained relatively high and constant for continuing users

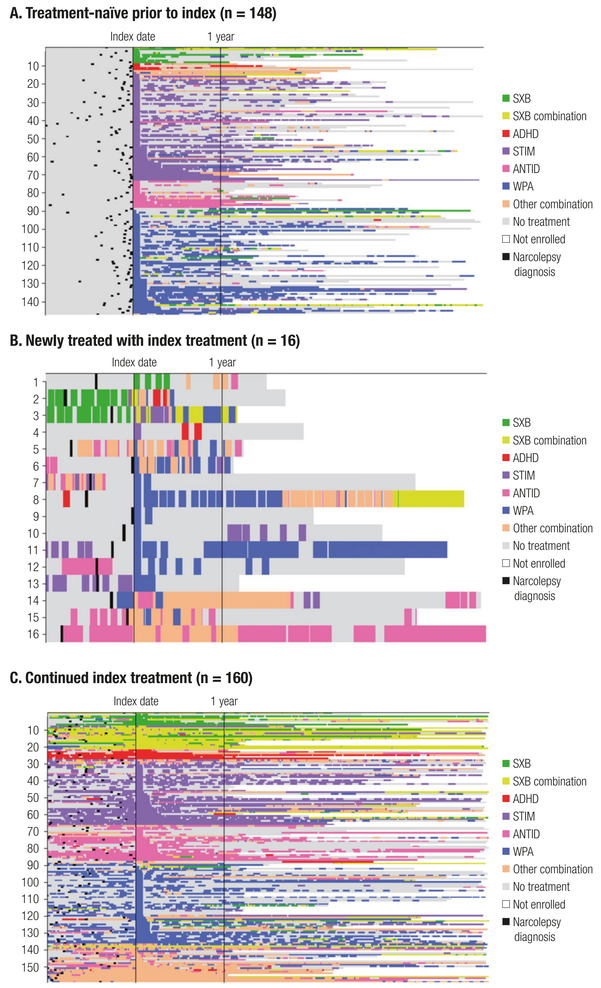
Figure 4. Time to Discontinuation of SXB for New and Continuing Users



SXB, sodium oxybate; CI, confidence interval.

- The median (95% confidence interval) time to SXB discontinuation was 341 (147, not reached) days for new users and was not reached within the time studied for continuing users

Figure 5. GRAPHx Patterns of Narcolepsy-related Treatment for Patients Who Were Treatment-naïve Prior to Index, Were Newly Treated With Index Treatment, and Continued Users at Index[a]



SXB, sodium oxybate; ADHD, attention-deficit/hyperactivity disorder; STIM, stimulant; ANTID, antidepressant; WPA, wake-promoting agent.

[a]Multicoloured line segments represent different treatments received since the index date. The presence and length of segments and changes in colours and patterns over time indicate various treatment episodes. Each horizontal line represents an individual patient's treatment history in the follow-up period, and the height of each coloured section is proportional to the total number of patients receiving each treatment. Grey areas represent periods of enrolment during which there were no claims for the treatments of interest.

- In all treatment groups (**Figures 5A-C**), interruptions in treatment use were common in the first year after the index date; however, many patients appeared to resume the treatment at the index date after an interruption, indicating persistence in use
  - In contrast, switching patterns seemed infrequent across treatments at the index date (**Figures 5A-C**)
  - Due to a very small sample size, the panel containing data for paediatric patients newly treated with index treatment (**Figure 5B**) could not be interpreted
- Adherence to the treatments at the index date (uninterrupted line segment) appeared more common among those who continued the treatment at the index date (**Figure 5C**) compared to treatment-naïve patients (**Figure 5A**), which may suggest improved tolerability or dosing adjustment after continued exposure to treatment; this pattern was sharpest among users taking SXB
- For treatment-naïve patients (**Figure 5A**), the most common treatment at the index date was an ADHD stimulant, followed by a WPA, an antidepressant, a nonstimulant ADHD agent, and SXB

Limitations

- The study population primarily represents a commercially insured segment of the US population; results may not be generalizable to all patients with narcolepsy
- Claims-based analyses are limited by the possibility of diagnosis coding errors; however, concomitant requirements for MSLT and narcolepsy diagnosis codes may reduce this risk

Conclusions

- In real-world settings in the United States, SXB adherence and persistence rates were generally high in paediatric patients with narcolepsy over the 1-year assessment period
- High rates of adherence (mean PDC, 60%-89% and PDC ≥80%, 44%-83%) and persistence were observed for new and continuing SXB users relative to rates reported in the literature for other treatments[5-7]
  - Adherence for stimulants and nonstimulants for ADHD (1 year mean medication possession ratio, 0.57 [stimulants] and 0.49 [nonstimulants])[5]
  - Adherence for antidepressants for major depressive disorder (PDC ≥80% at 1 year, 26%)[7]
- Adherence rates were lower and persistence rates were similar for new versus continuing users
- These findings are consistent with data from clinical trials showing that titration to an optimal SXB dose, which may involve multiple steps, is critical in achieving an optimal response, which may take up to 2 months.[4,8-10] Moreover, adverse events with SXB are known to occur early and diminish over time.[10] Once optimal dosing is established, as with continuing users in this study, patients can achieve and maintain long-term treatment benefits[8,10-12]

References: 1. Thorpy MJ, Krieger AC. *Sleep Med.* 2014;15(5):502-507. **2.** Morgenthaler TI, et al. *Sleep.* 2007;30(12):1705-1711. **3.** Plazzi G, et al. *Lancet Child Adolesc Health.* 2018;2(7):483-494. **4.** Plazzi G, et al. *Sleep.* 2019;42(suppl_1):A307-A308. **5.** Gajria K, et al. *Neuropsychiatr Dis Treat.* 2014;10:1543-1569. **6.** Yeaw J, et al. *J Manag Care Pharm.* 2009;15(9):728-740. **7.** Keyloun KR, et al. *CNS Drugs.* 2017;31(5):421-432. **8.** Bogan RK, et al. *J Clin Sleep Med.* 2015;11(4):427-432. **9.** Thorpy MJ, et al. *Sleep Med.* 2015;16(1):9-18. **10.** XYREM® (sodium oxybate) oral solution [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2018. **11.** Mignot E, et al. *Sleep.* 2018;41(suppl_1):A302. **12.** Mignot E, et al. *Sleep.* 2019;42(suppl_1):A308.

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