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Yves Dauvilliers, Anne Marie Morse, Patricia Chandler, Amy Desmarais & Richard K. Bogan

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Future NEUROLOGY

Plain Language Summary of Publication

Low-sodium oxybate improved symptoms in adults with idiopathic hypersomnia: a plain language summary of publication

Yves Dauvilliers, MD, PhD[1]; Anne Marie Morse, DO[2]; Patricia Chandler, MD[3]; Amy Desmarais, MSA[4]; Richard K. Bogan, MD[5]
Full list of affiliations can be found at the end of the article.

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Where can I find the original article on which this summary is based?

The original article, 'Safety and efficacy of lower-sodium oxybate in adults with idiopathic hypersomnia: a phase 3, placebo-controlled, double-blind, randomised withdrawal study,' can be accessed using the link below. The article is available for a fee. https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(21)00368-9/fulltext

Summary

What is this summary about?

This is a plain language summary of a clinical study of a medicine called low-sodium oxybate (or LXB, also known as Xywav®) in adults with idiopathic hypersomnia.

Idiopathic hypersomnia is a rare sleep disorder that makes people have extreme sleepiness during the day. It also can make them sleep a long time at night and during the day, and make it hard for them to fully wake up.

How to say (double-click on the icon to play sound)…

- **Idiopathic hypersomnia:** i-dee-uh-PA-thik hai-pur-SAAM-nee-uh
- **Sleep inertia:** sleep uh-NUR-shuh
- **Oxybate:** AAK-see-bayt

This study looked at changes in idiopathic hypersomnia symptoms after participants took LXB for 12 to 16 weeks, and then either switched to placebo for 2 weeks or kept taking LXB for 2 more weeks. The placebo did not contain any medicine, but it looked and tasted like LXB. By comparing results from the placebo and LXB groups, researchers could see if LXB helped symptoms of idiopathic hypersomnia, as well as the impacts of those symptoms on day-to-day functioning and quality of life.

What were the results?

In this study, excessive daytime sleepiness and other symptoms of idiopathic hypersomnia (like prolonged sleep and **sleep inertia**), and the impacts of these symptoms on day-to-day functioning and quality of life, got worse for participants who switched from LXB to placebo compared with those who kept taking LXB. In other words, LXB helped treat symptoms of idiopathic hypersomnia, including excessive daytime sleepiness. The most common **side effects** were nausea, headache and dizziness.

Sleep inertia: Difficulty in waking up and becoming fully alert after sleeping. People with sleep inertia may sleep through multiple alarms and need help from another person to wake up.
Side effects: Unexpected medical events that happen while taking a medicine.

What do the results mean?

LXB reduced excessive daytime sleepiness and other symptoms (like prolonged sleep and sleep inertia) in participants with idiopathic hypersomnia, and also improved their day-to-day functioning and quality of life.

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The purpose of this plain language summary is to help you understand the findings from recent research

LXB is approved to treat adults with idiopathic hypersomnia, which is what was studied, as discussed in this summary. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not on the results of a single study.

Who is this article for?

This article is for people who have idiopathic hypersomnia or know/take care of someone with idiopathic hypersomnia, and want to understand how a medicine called LXB can help treat them or their loved one.

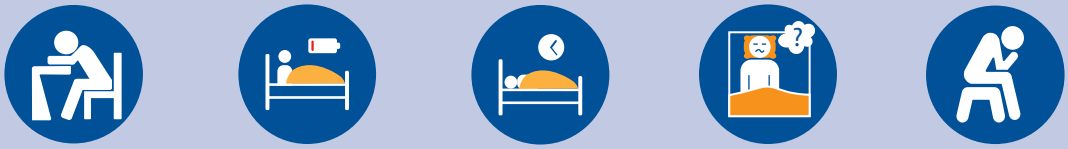
Who sponsored this study?

This study was **sponsored** by Jazz Pharmaceuticals.

Sponsor: A sponsor is a company or organization that oversees and pays for a clinical research study. The sponsor also collects and analyzes the information that is generated during the study.

What is idiopathic hypersomnia?

- Idiopathic hypersomnia is a rare sleep disorder that currently does not have a cure.
- People with idiopathic hypersomnia have extreme sleepiness during the day. They may fall asleep even when they are trying to stay awake. Although they get enough hours of sleep at night, often this sleep is not refreshing, and naps usually are not helpful in lowering excessive daytime sleepiness.
- Some people with idiopathic hypersomnia sleep for a long time (11 hours or more during a 24-hour period) but still feel they need more sleep.
- People with idiopathic hypersomnia may have sleep inertia.
- People with idiopathic hypersomnia may find it hard to go to school, keep a job or have good social relationships and quality of life.



Excessive daytime sleepiness

Unrefreshing sleep at night and in daytime naps

Prolonged nightime sleep

Sleep inertia

Decreased quality of life, work and social relationships

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How is idiopathic hypersomnia usually treated?

LXB is approved in the United States for the treatment of idiopathic hypersomnia in adults. The generic name of LXB is calcium, magnesium, potassium and sodium oxybates oral solution.

LXB is currently the only medicine approved for treating idiopathic hypersomnia in the United States.

LXB is also approved for the treatment of cataplexy or excessive daytime sleepiness in people with narcolepsy who are 7 years of age or older.

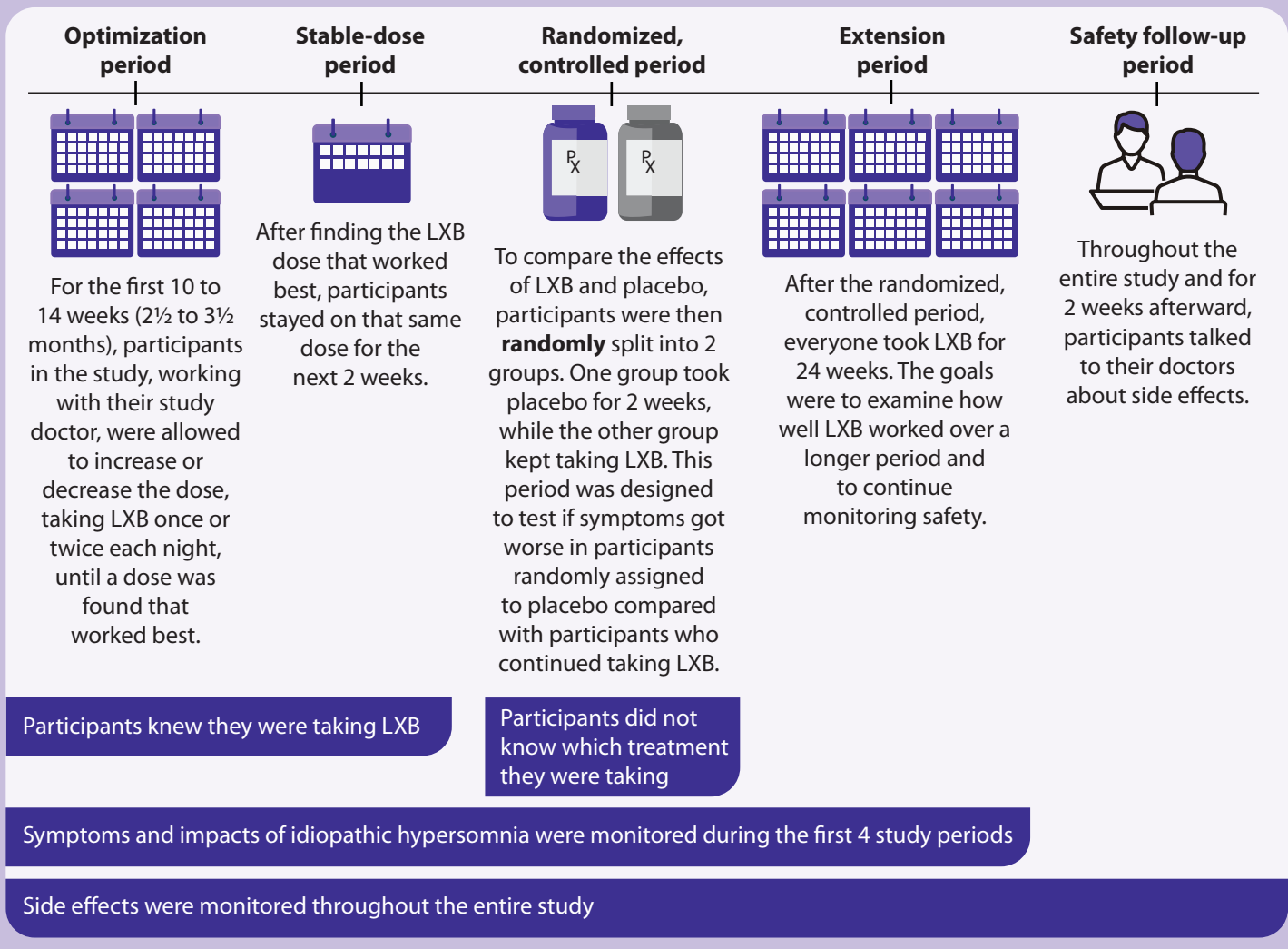
Doctors sometimes prescribe treatments that, though not approved for idiopathic hypersomnia, may help ease symptoms like excessive daytime sleepiness. These treatments include stimulants (such as amphetamine and methylphenidate) and wake-promoting medicines (such as modafinil and solriamfetol). Less often, other medicines like sodium oxybate (SXB) may be used. SXB has the same active ingredient as LXB but contains much more sodium. The American Heart Association and other health organizations recommend reducing daily sodium intake to help reduce the risk of heart disease.

Why was this study done?

The study was done to see whether LXB treatment helps reduce excessive daytime sleepiness and other symptoms of idiopathic hypersomnia.

How was this study done?

- Participants in the study were adults (18 to 75 years old) with idiopathic hypersomnia who slept 7 or more hours at night on average. Some participants were taking other medicines for their idiopathic hypersomnia symptoms. Other participants were not taking any medicine for idiopathic hypersomnia. At each place where the study was done, the study plan was approved by a group called an independent ethics committee or an institutional review board.
- At the start of the study, participants taking SXB switched to the same dose of LXB, and participants not taking SXB started taking LXB at the recommended starting dose. Participants taking alerting agents (stimulants or wake-promoting medicines) at the start of the study took those medicines during the entire study.



Optimization: The process of trying different doses of a medicine to find the dose that works best.
Randomly: Study participants were assigned to different groups by chance.

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What did the study look at?

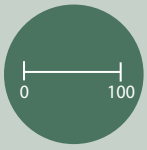
- During the optimization and stable-dose periods, researchers looked at changes in severity of idiopathic hypersomnia symptoms while everyone was taking LXB.
- During the randomized, controlled period, researchers compared participants who switched from LXB to placebo with participants who kept taking LXB. Remember, participants were not told if they were taking LXB or placebo during this time.

Several things were measured, including:

Excessive daytime sleepiness. Participants filled out a questionnaire called the Epworth Sleepiness Scale, which asked how likely they were to fall asleep in different situations.

Overall symptoms and impacts of idiopathic hypersomnia. Participants filled out the Idiopathic Hypersomnia Severity Scale, which is a questionnaire that asked about their excessive daytime sleepiness, sleep inertia and amount of time spent sleeping at night and during the day. It also asked about the effects of these symptoms on their day-to-day activities.

How well participants in the study and their doctors thought LXB worked overall. Participants in the study filled out the Patient Global Impression of Change questionnaire. Their doctors filled out the Clinical Global Impression of Change questionnaire. These questionnaires asked to what extent the condition of participants in the study improved, got worse or stayed the same.



Sleep inertia. Each morning, participants rated their difficulty awakening on a scale ranging from 0 (very easy) to 100 (very difficult). This measure was called the visual analog scale for sleep inertia.

Day-to-day functioning and quality of life. Participants filled out a questionnaire called the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem, which asked about their impairment at work and in general activities (including school) due to symptoms of idiopathic hypersomnia. Scores are presented as percentages, from 0% (no impairment) to 100% (completely impaired). Participants also completed the Functional Outcomes of Sleep Questionnaire, which asked about difficulty carrying out certain activities because of being too sleepy or tired. Scores range from 5 (more difficult) to 20 (less difficult).

Safety. Side effects were monitored throughout the study.

Results

154 participants started the study and took LXB at least once

123 finished the optimization period

115 finished the stable-dose period, entered the randomized, controlled period and were included in the analysis; 8 study participants did not meet criteria to continue in the study or dropped out due to side effects or other reasons

Study participants

40 years old on average

68% female

32% male

84% White

6% Black

1% other/multiple

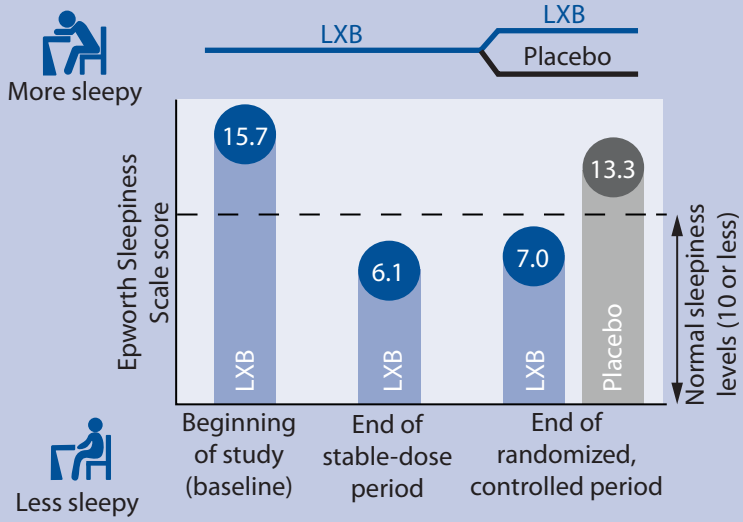
9% declined to state

68% from North America

32% from Europe

Excessive daytime sleepiness

- During the randomized, controlled period, excessive daytime sleepiness got worse for participants who switched from LXB to placebo, but stayed similar for participants who kept taking LXB.
- Excessive daytime sleepiness was measured with the Epworth Sleepiness Scale (score range, 0 to 24).
- This finding was statistically significant, meaning that it was most likely related to participants switching off the active medicine, from LXB to placebo, and not due to chance.



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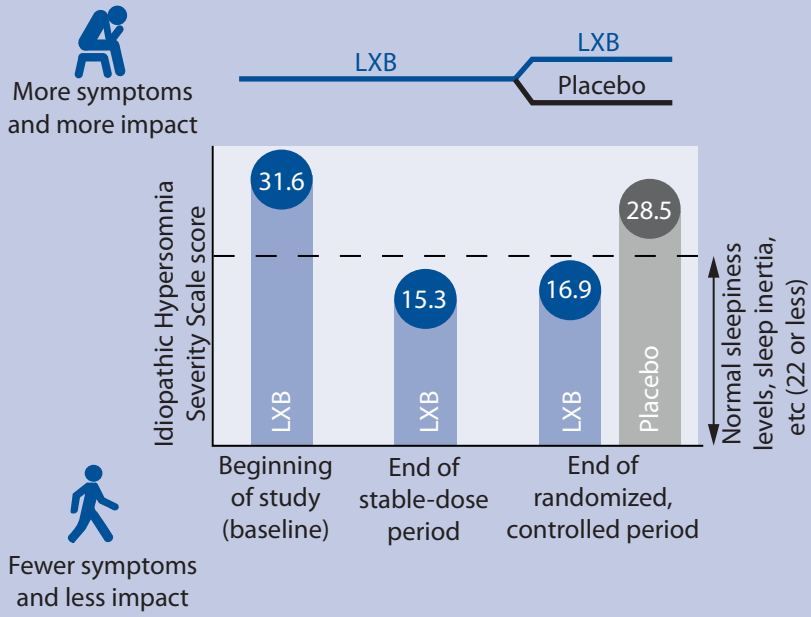
Overall symptoms and impacts of idiopathic hypersomnia

- During the randomized, controlled period, overall symptoms and impacts of idiopathic hypersomnia got worse for participants who switched from LXB to placebo, but stayed similar for participants who kept taking LXB.
- Symptoms and impact were measured with the Idiopathic Hypersomnia Severity Scale (score range, 0 to 50).
- These findings, like the findings related to excessive daytime sleepiness, were statistically significant.

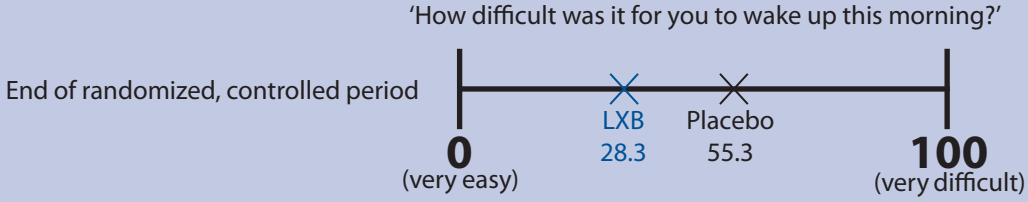


How well participants in the study and their doctors thought LXB worked overall

Using questionnaires called the Patient Global Impression of Change and the Clinical Global Impression of Change, most participants in the placebo group (88%) and their doctors (88%) said idiopathic hypersomnia symptoms got worse when the participants stopped taking LXB during the randomized, controlled period (when they did not know which treatment they were taking). Fewer participants in the LXB group (21%) and their doctors (21%) said idiopathic hypersomnia symptoms got worse while the participants kept taking LXB during the randomized, controlled period.

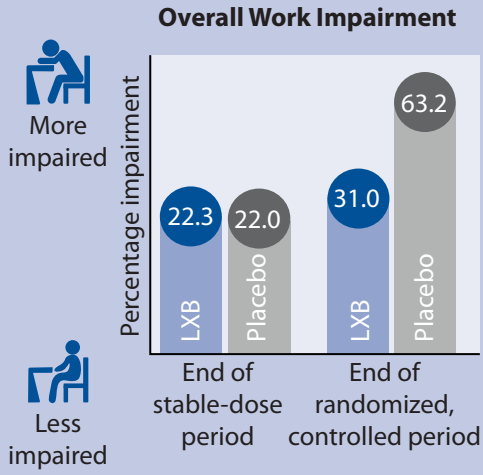
Sleep inertia

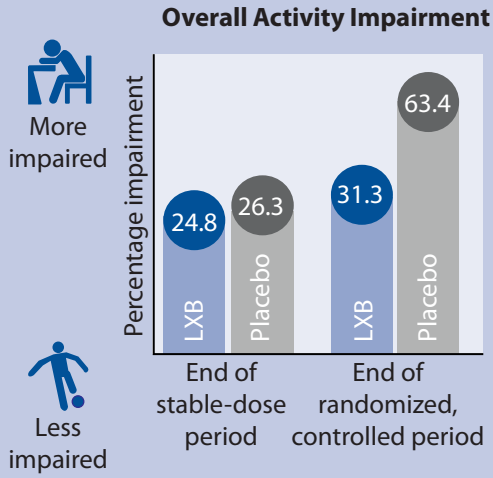
Sleep inertia (using the visual analog scale for sleep inertia, in response to the question, 'How difficult was it for you to wake up this morning?') got worse after participants switched from LXB to placebo, but stayed similar for participants who kept taking LXB.

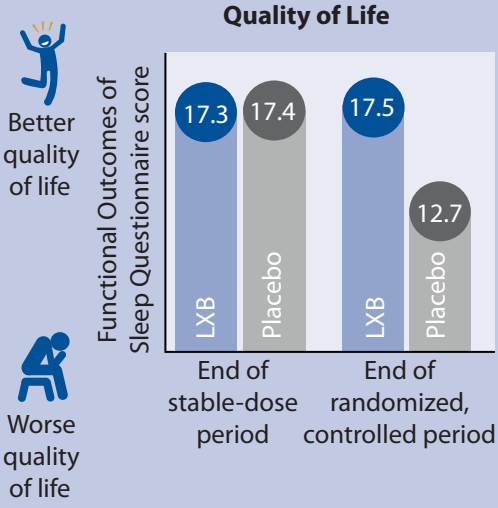


Day-to-day functioning and quality of life

- Overall functioning at work and in general activities (using the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem) got worse for participants who switched from LXB to placebo, but stayed similar for participants who kept taking LXB. This also happened for absenteeism (missing work) and presenteeism (being at work but not functioning well).
- Quality of life (using the Functional Outcomes of Sleep Questionnaire) got worse for participants who switched from LXB to placebo, but stayed similar for participants who kept taking LXB.

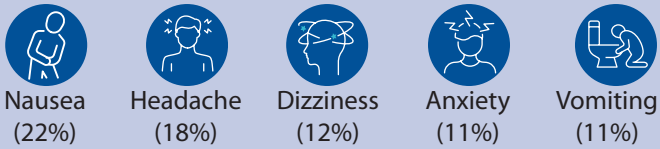






Safety

- The most common side effects with LXB, each reported by 10% or more of participants treated with LXB.



- 20% of participants reported no side effects while taking LXB.

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What do the results of this study mean?

- This study showed that LXB helps treat symptoms of idiopathic hypersomnia.
- When participants in the study switched from LXB to placebo, their excessive daytime sleepiness, overall idiopathic hypersomnia symptoms and sleep inertia got worse, and so did the impacts of these symptoms on their functioning and quality of life. This means that LXB effectively treats symptoms of idiopathic hypersomnia, including excessive daytime sleepiness and sleep inertia.
- When the switch was made from LXB to placebo, a majority of the participants in the study and their doctors said that idiopathic hypersomnia symptoms got worse.
- Based on the side effects reported, the safety of LXB in this study was similar to the safety in a previous study that was done with LXB for narcolepsy.

Where can readers find more information?

This study began on November 27, 2018 and ended on December 18, 2020. No additional similar studies are planned. The original article, titled 'Safety and efficacy of lower-sodium oxybate in adults with idiopathic hypersomnia: a phase 3, placebo-controlled, double-blind, randomised withdrawal study,' was published in the medical journal *Lancet Neurology* in 2022: Dauvilliers Y, Arnulf I, Foldvary-Schaefer N *et al. Lancet Neurol.* 21(1), 53–65 (2022).

You can access the article using the link below. The article is available for a fee at: https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(21)00368-9/fulltext

The United States Food and Drug Administration requires that clinical trials be registered on the ClinicalTrials.gov website. You can find more information about this trial here: https://clinicaltrials.gov/study/NCT03533114

For additional information about idiopathic hypersomnia, or to get support or involved, please visit the website of the Hypersomnia Foundation, a 501(c)(3) nonprofit organization dedicated to improving the lives of people with idiopathic hypersomnia and related sleep disorders: https://www.hypersomniafoundation.org/ih/

Affiliations

[1]Sleep and Wake Disorders Centre, Department of Neurology, Gui de Chauliac Hospital, Montpellier, France; University of Montpellier, INSERM Institute Neuroscience Montpellier, Montpellier, France (y-dauvilliers@chu-montpellier.fr); [2]Janet Weis Children's Hospital, Geisinger Medical Center, Danville, PA, USA (amorse@geisinger.edu); [3]Jazz Pharmaceuticals, Palo Alto, CA, USA (patricia.chandler@jazzpharma.com); [4]Hypersomnia Foundation, Inc., Atlanta, GA, USA (amy@hypersomniafoundation.org); [5]University of South Carolina School of Medicine, Columbia, SC, USA (richard.bogan@bogansleep.com)

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Competing interests disclosure

A Desmarais is Treasurer/Chief Financial Officer of the Hypersomnia Foundation, a 501(c)(3) nonprofit organization. The authors have no other competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

Writing disclosure

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