Future NEUROLOGY

Plain Language Summary of Publication

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

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First draft submitted: 11 August 2023; Accepted for publication: 13 November 2023; Published online: 18 January 2024

Summary

What is this summary about?

This plain language summary describes a clinical study that looked at the effects of a medicine called low-sodium oxybate (or LXB; XYWAV® [calcium, magnesium, potassium, and sodium oxybates]) in adults with narcolepsy. Narcolepsy is a rare brain disorder that can make people feel extremely sleepy during the day or have symptoms like cataplexy, which is sudden and temporary muscle weakness. This study compared changes in symptoms between people who either switched to placebo or continued with LXB after they had been taking LXB for 14 weeks. The placebo looked and tasted like LXB but did not have the active ingredient. This allowed researchers to see if LXB improved symptoms like cataplexy and extreme daytime sleepiness.

How to say (double click to play sound)...

- **Cataplexy**: KAT-uh-plek-see
- **Narcolepsy**: NAAR-kuh-lep-see
- **Oxybate**: AAK-si-bayt

What were the results?

Cataplexy and daytime sleepiness got worse in people who switched to placebo compared with those who kept taking LXB. This means that LXB worked well to treat symptoms of cataplexy and extreme daytime sleepiness. The most common side effects–defined as any unexpected medical events that happened while taking LXB–were headache, nausea, and dizziness.

What do the results mean?

LXB lowered the symptoms of cataplexy and daytime sleepiness in people with narcolepsy. LXB is approved in the USA to treat cataplexy or extreme daytime sleepiness (in people with narcolepsy who are 7 years of age and older). LXB is approved in Canada to treat cataplexy in adults with narcolepsy.

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

The original article is called 'Efficacy and safety of calcium, magnesium, potassium, and sodium oxybates (lower-sodium oxybate [LXB]; JZP-258) in a placebo-controlled, double-blind, randomized withdrawal study in adults with narcolepsy with cataplexy,' and it can be read for free here: https://academic.oup.com/sleep/article/44/3/zsaa206/5923328.

Who is this article for?

This article is for people who have narcolepsy, or know/care for someone with narcolepsy, and want to know how well a medicine called LXB works.

Future Medicine part of fsg

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

LXB is used to treat the condition under study that is discussed in this summary. Approval varies by country; please check with your local provider for more details. 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 sponsored this study?

Jazz Pharmaceuticals **sponsored** this study.

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 narcolepsy with cataplexy?

- Narcolepsy is a rare brain disorder with no known cure. There are two types of narcolepsy, called narcolepsy type 1 and narcolepsy type 2. They are similar except that only people with narcolepsy type 1 have cataplexy.
- Cataplexy, which is sudden loss of muscle control triggered by emotions, is different for every person. Some cataplexy attacks might affect face muscles, or cataplexy could also cause a person to collapse. Some people have cataplexy attacks more than once per day, and some rarely have them.
- Another main narcolepsy symptom is having extreme sleepiness during the day. People with narcolepsy can also have disruptions in nighttime sleep, hallucinations, or sleep paralysis, which is being unable to move upon awakening or falling asleep.
- These symptoms can make it hard for people with narcolepsy to have a good quality of life and work well at a job or in school. It can also have negative effects on their social relationships.

Cataplexy

Extreme daytime sleepiness

Disrupted nighttime sleep

Sleep-related hallucinations

Sleep paralysis

How is narcolepsy with cataplexy usually treated?

Most narcolepsy medicines only treat daytime sleepiness or cataplexy, but not both, or have not been studied very much.

Alerting agents

Some doctors prescribe wake-promoting medicines, like modafinil, or stimulant medicines, like methylphenidate or amphetamine, to treat daytime sleepiness. These medicines signal the brain to be alert.

Antidepressants

Antidepressants are also used to treat cataplexy, but there is not very much known about how well they work and how safe they are for people with narcolepsy with cataplexy.

Pitolisant

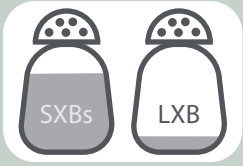
A newer medicine called pitolisant can help with cataplexy and daytime sleepiness.

Other medicines, high-sodium oxybates (SXBs), include Xyrem® and Lumryz™, and are approved to treat the following:

Cataplexy or extreme daytime sleepiness in people with narcolepsy (in adults for Lumryz™ and people ≥7 years for Xyrem®)

SXB medicines work well to treat daytime sleepiness and cataplexy, but contain a lot of sodium, which can cause more long-term problems like high blood pressure.

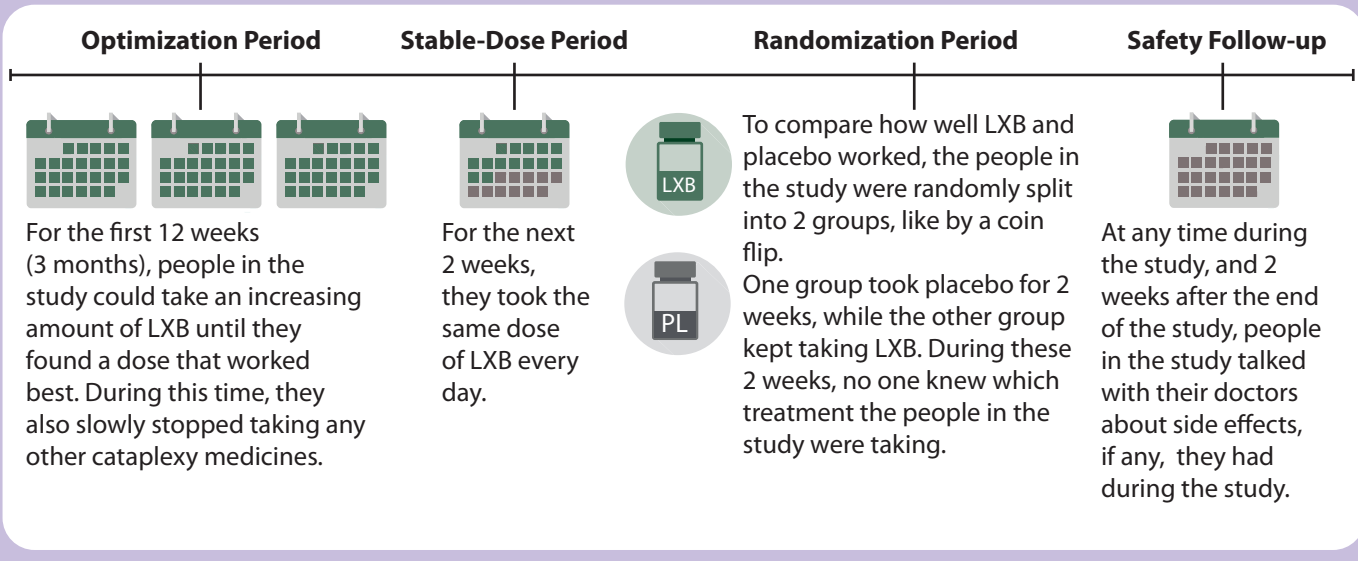
LXB is like SXB medicines but with much less sodium



LXB is a medicine that has the same active ingredient as SXB medicines, but with 92% less sodium. The removal of almost all the sodium may be important in people with narcolepsy and could make LXB safer than high-sodium oxybate medicines.

How was the study done?

This study involved adults (18–70 years old) with narcolepsy type 1 who usually had 14 cataplexy attacks in a 2-week period. They could be taking any medicines, or none, for their narcolepsy at the start of the study.



What did the study look at?

Researchers looked at changes from the time when people in the study switched from LXB to placebo to see if their symptoms got worse. This change was compared with the change in people who carried on taking LXB to see what the differences were.

People in the study used diaries to document the number of cataplexy attacks they had each day. Researchers used the diaries to look for changes in the number of weekly cataplexy attacks, as well as the number of days without cataplexy attacks.

This study also looked at the change in sleepiness using the Epworth Sleepiness Scale, which is a questionnaire that asked how likely people were to fall asleep in certain situations.

This study also examined how well people in the study and their doctors thought LXB worked overall.

- People in the study filled out the Patient Global Impression of Change (PGIc) questionnaire. Their doctors filled out the Clinical Global Impression of Change (CGIc) questionnaire. The PGIc and CGIc look at changes in overall narcolepsy symptoms.
- Two different questionnaires asked people how they felt overall:
  - the 36-Item Short-Form Health Survey Version 2 (SF-36)
  - the EuroQoL (EQ-5D-5L)

Side effects were looked at throughout the study.

Results

201 people

37 years old on average

61% female

88% White

61% Europe
39% North America

155 finished the optimization period

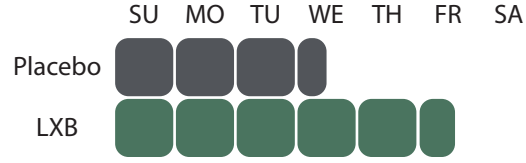
149 went into the stable-dose period

Cataplexy

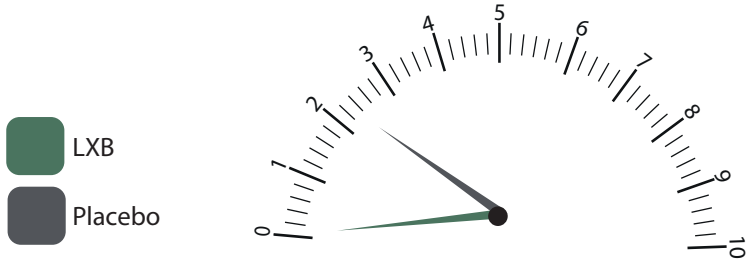
During the randomization part of the study, the number of weekly cataplexy attacks went up for people who switched to placebo.

- The average difference between LXB and placebo was statistically significant. This means that it probably was not due to chance. When patients stopped taking LXB, their cataplexy symptoms returned.

People who switched to placebo only had 3.5 days per week without a cataplexy symptom at the end of the randomization period.



People who kept taking LXB had an average of 5.6 days a week without a cataplexy symptom.

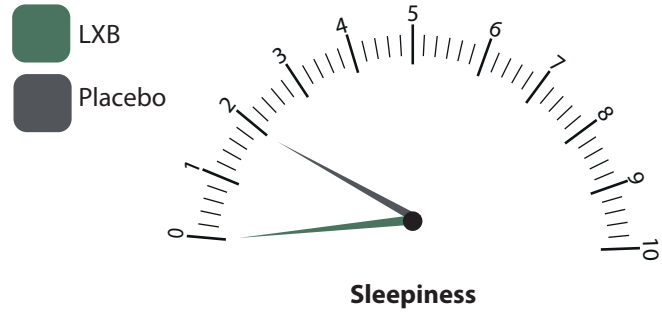


Weekly cataplexy attacks

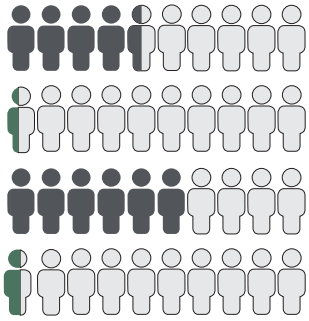
Daytime sleepiness (Epworth Sleepiness Scale)

Daytime sleepiness got worse for people who switched to placebo, but stayed the same for those who kept taking LXB.

- The average difference between LXB and placebo was statistically significant. This means that it probably was not due to chance. When people stopped taking LXB, their sleepiness symptoms came back.



How well LXB worked overall



At the end of the randomization period, almost half (45%) of people in the placebo group said their narcolepsy was 'much worse' or 'very much worse' compared with only 4% in the LXB group.

60% of doctors of people who took the placebo said their patients' narcolepsy was 'much worse' or 'very much worse' compared with only 6% in the LXB group.

On the SF-36 and EQ-5D-5L questionnaires, people reported that their overall health got worse when taking placebo, but not LXB.

Those who kept taking LXB did not report that their physical or mental state got worse. Those taking placebo did.

Safety

Common side effects of LXB:

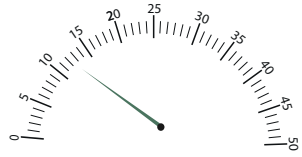

Headache

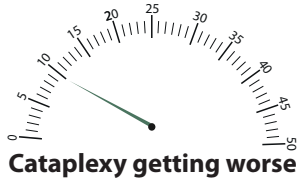

Nausea

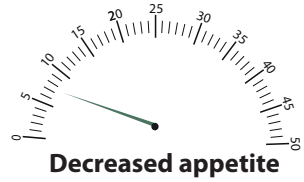

Dizziness

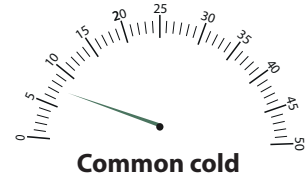

24% of all people in the study did not report any side effects.

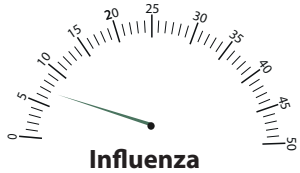
Percent of people with side effects while taking LXB:











What do the results of this study mean?

This study showed that LXB helps treat cataplexy and daytime sleepiness in people with narcolepsy with cataplexy.

Many people with narcolepsy already take medicine for their cataplexy. This study allowed people who were already taking such medicines to take part in the study by slowly stopping those treatments as they started their treatment with LXB. This is probably how most doctors would treat such patients.

- When people stopped taking LXB and started taking placebo, their daytime sleepiness and cataplexy got worse.
- Most people and their doctors said that narcolepsy symptoms got 'much worse' or 'very much worse' when the people switched from LXB to the placebo.
- Side effects of LXB were similar to those seen with SXB.

LXB is important because it has 92% less sodium than SXB medicines, and it might be safer.
This is because taking a lot of sodium increases the risk of heart disease and other health conditions.

Where can readers find more information on this study?

The original article was published in the medical journal *Sleep* in 2021. The title is "Efficacy and safety of calcium, magnesium, potassium, and sodium oxybates (lower-sodium oxybate [LXB]; JZP-258) in a placebo-controlled, double-blind, randomized withdrawal study in adults with narcolepsy with cataplexy." Bogan RK, Thorpy MJ, Dauvilliers Y et al. *Sleep*. 44(3), zsaa206 (2021).
You can access and read the article for free using the links below:
https://academic.oup.com/sleep/article/44/3/zsaa206/5923328
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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/ct2/show/NCT03030599

For additional information about narcolepsy, or to get support or involved, please visit Wake Up Narcolepsy, a 501(c)(3) not-for-profit organization dedicated to driving narcolepsy awareness, education, and research at their website:
www.wakeupnarcolepsy.org/

Acknowledgments
The authors would like to thank the people who participated in this study, as well as their families.

Financial disclosure
RK Bogan has served on the speakers' bureau and participated in advisory boards for Jazz Pharmaceuticals and Harmony Biosciences and has received research/grant support from Jazz Pharmaceuticals, Harmony Biosciences, Balance Therapeutics, Axsome Therapeutics, Merck, and Avadel Pharmaceuticals. MJ Thorpy has received research/grant support and consultancy fees from Jazz Pharmaceuticals, Harmony Biosciences, Balance Therapeutics, Axsome Therapeutics, and Avadel Pharmaceuticals. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Competing interests disclosure
N Foldvary-Schaefer has served on an advisory committee for Jazz Pharmaceuticals and participated in clinical trials for Suven, Takeda, and Vanda. W Macfadden is an employee of Jazz Pharmaceuticals who, in the course of his employment, has received stock options exercisable for, and other stock

awards of, ordinary shares of Jazz Pharmaceuticals plc. M Gow is the co-founder and executive director of Wake Up Narcolepsy, a 501(c)(3) not-for-profit 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

Under the direction of the authors, Benjamin Hiller, PhD, and Emily Bruggeman, PhD, of Peloton Advantage, LLC, an OPEN Health company, provided medical writing and editorial support for this manuscript, which was funded by Jazz Pharmaceuticals.