Clinical Study Results

Inspired by patients. Driven by science.

Study Sponsor: UCB Biopharma SRL

Drug Studied: Fenfluramine

Protocol Number: ZX008-1601 (EP0214)

Short Study Title: A study to learn how well fenfluramine works and how safe it is in children and young adults with Lennox-Gastaut syndrome

Thank you

UCB thanks all the participants of this study and their caregivers. All the participants and caregivers helped the researchers learn more about using fenfluramine hydrochloride in people with Lennox-Gastaut syndrome. Fenfluramine hydrochloride is also called ZX008. In the rest of this summary, fenfluramine hydrochloride will be called **fenfluramine**.

This is a summary of the main results of this study. An independent, non-profit organization helped prepare this summary of the study results, which included feedback from patients.

We think it is important to share the results with the participants, their caregivers, and the public. We hope this summary helps the participants and their caregivers understand their important role in medical research.

The purpose of this summary is only to share information. If you or the child you care for needs medical advice, please contact your or your child's doctor. If you or the child in your care participated in this study and has questions about the results, please speak with study staff.

This summary was approved by UCB Biopharma SRL on 9 June 2025.
The information in this summary is current as of this date.

Overview of this study

Why was the research needed?

Researchers are looking for a different way to treat Lennox-Gastaut syndrome (LGS). Before a drug is available for all patients, researchers do clinical studies to find out how the drug works and how safe it is.

What treatments did the participants take?

This study had 2 cohorts (groups) of participants called **Cohort A** and **Cohort B**. Cohort A included participants from North America, Europe, and Australia. Cohort B included only participants from Japan.

Each cohort of this study had 2 parts. In **Part 1** of the study, the participants took either fenfluramine or a placebo. A placebo looks like a drug but does not have any medicine in it. In **Part 2** of the study, all of the participants took fenfluramine.

What were the results of this study?

The main question the researchers wanted to answer in this study was:

- **Did fenfluramine help the participants have fewer seizures?**
  - **Yes.** In Part 1, the participants in Cohort A who took fenfluramine had fewer seizures than the participants in Cohort A who took the placebo. Cohort A included most of the participants in this study.

More details about the results of this study are included later in this summary.

What medical problems did the doctors report as possibly related to study treatment?

The number of participants who had medical problems that the study doctors reported as possibly related to the study treatment is in the table below:

	Part 1	Part 2
Cohort A	46.0% (121 out of 263 participants)	42.9% (106 out of 247 participants)
Cohort B (Japan)	51.5% (17 out of 33 participants)	65.6% (21 out of 32 participants)

The most common possibly related medical problem was decreased appetite.

Where can I learn more about this study?

You can find more information about this study on the websites listed on the last page. If a report of the study results is available, it can also be found on those websites.

Why was the research needed?

Before a treatment is available to the public, researchers do clinical studies to get information about how well the treatment works and about how safe it is.

The researchers in this study wanted to learn if fenfluramine worked in a large number of participants living with **Lennox-Gastaut syndrome** (**LGS**). They also wanted to learn if the participants had any medical problems during the study.

LGS is a severe type of epilepsy. People with epilepsy often get sudden bursts of activity in their brains called **seizures**. Seizures can cause intense discomfort and uncontrollable movements. Symptoms of LGS usually start before the age of 11. As people with LGS get older, the disease can also cause problems with their behavior and brain function.

People with LGS often have seizures that cause their head or their whole body to drop uncontrollably. These are called **drop seizures**. Drop seizures are often short, but severe, and can sometimes cause injury and death.

When this study began, there were other treatments available for LGS, but those did not work well enough for everyone. The study drug **fenfluramine** was designed to affect specific cells in the brain that are related to seizures. So, researchers thought that fenfluramine could help to reduce the number of drop seizures in people with LGS.

What was the main question studied?

The main question the researchers wanted to answer in this study was:

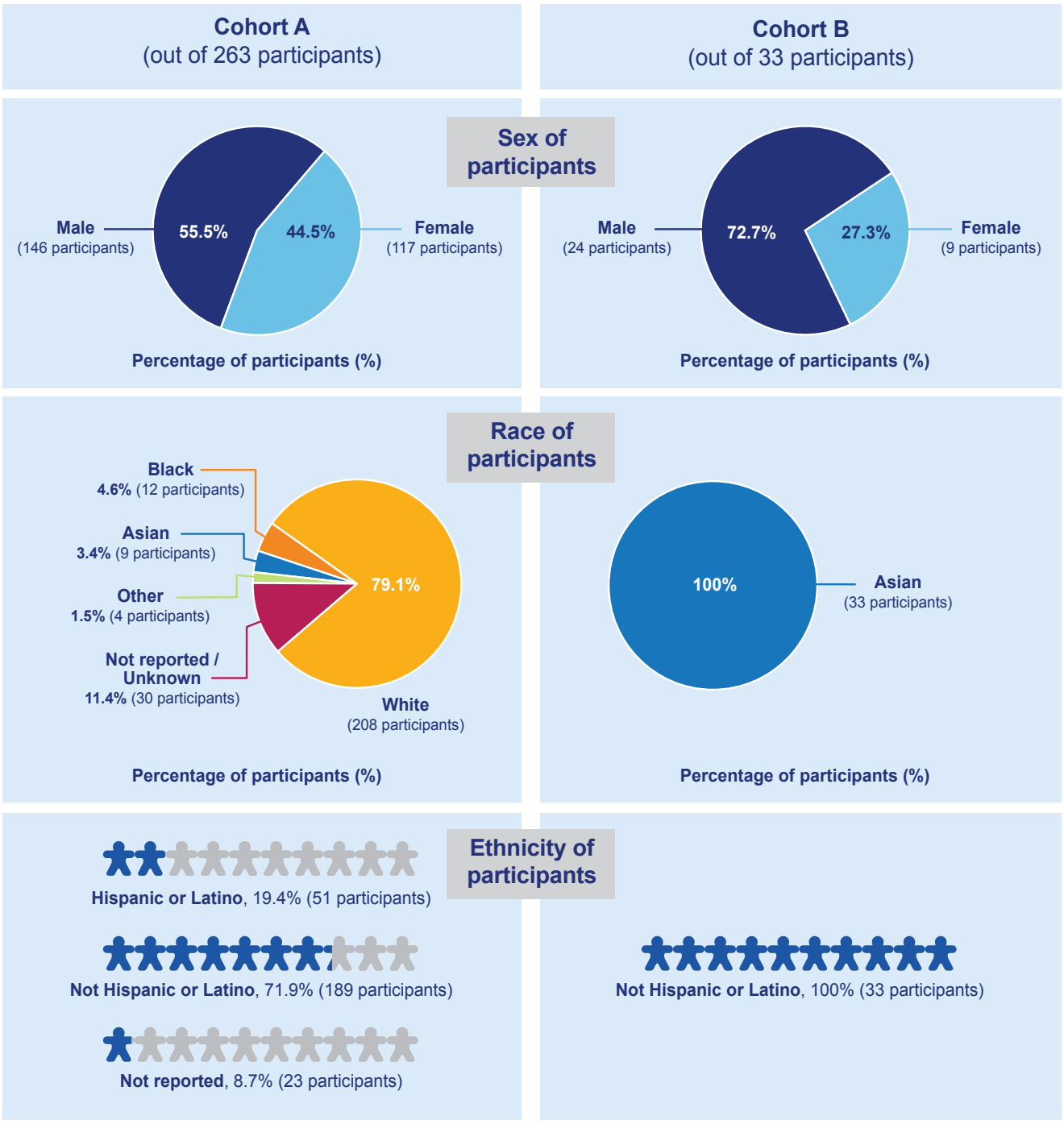
- Did fenfluramine help the participants have fewer seizures?

The researchers also wanted to know what medical problems happened that were possibly related to study treatment.

Who participated in the study?

There were 263 participants with LGS who participated in **Cohort A** of this study, and there were 33 participants with LGS who participated in **Cohort B** of this study.

The participants in both cohorts were 2 to 35 years old when they joined.



LGS is more common in males than in females. This may explain why more males joined this study than females.

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The study included participants in 14 countries.

In this study, the researchers included participants living with LGS who:

- Started having seizures when they were 11 years old or younger
- Had at least 8 drop seizures in the 4 weeks before joining the study
- Had abnormal brain activity as measured by an electroencephalogram (EEG)
- Were taking between 1 and 4 drugs to control their seizures

Each participant was in part of this study for up to 20 weeks. Part 2 lasted up to 1 year for each participant in Cohort A, and up to 6 years for each participant in Cohort B. The whole study lasted about 6 and a half years. The study started in November 2017 and ended in May 2024.

What treatments did the participants take?

Fenfluramine can be made in 2 forms: fenfluramine hydrochloride, and fenfluramine base. The type of fenfluramine that participants took in these studies was **fenfluramine hydrochloride**. But, in this summary, fenfluramine hydrochloride is called fenfluramine.

The participants in this study took fenfluramine or a placebo as a liquid by mouth. The placebo looked like fenfluramine, but did not have any fenfluramine in it. The researchers used the placebo to better understand what effects may have been related to fenfluramine. Doses of fenfluramine were measured in milligrams per kilogram, also called mg/kg. This means that the amount of fenfluramine that the participants took each day was based on their body weight.

In this summary, “study treatment” means anything the participants took as a part of the study. This includes fenfluramine and the placebo. **Fenfluramine** is the drug that the researchers wanted to learn more about.

In **Part 1** of this study, none of the participants, caregivers, study doctors, or study staff knew what treatment each participant was taking. UCB staff also did not know. Some studies are done this way because knowing what treatment the participants are taking can affect the results of the study. After the study was completed, UCB learned what treatment each participant took so they could create a report of the results.

The researchers used a computer program to randomly choose if the participants took fenfluramine or the placebo in Part 1. This helped make sure the treatments were chosen fairly and comparing the results for the treatments was as accurate as possible.

In **Part 2** of this study, all of the participants took fenfluramine. During this part, the participants, study doctors, study staff, and UCB staff knew what the participants were taking.

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The chart below shows the treatments the researchers planned to study in **Part 1**:

	Placebo	Fenfluramine 0.2 mg/kg per day	Fenfluramine 0.8 mg/kg per day
	**Cohort A**: 87 participants **Cohort B**: 11 participants	**Cohort A**: 89 participants **Cohort B**: 11 participants	**Cohort A**: 87 participants **Cohort B**: 11 participants
	The **placebo** as a liquid taken by mouth	**Fenfluramine** as a liquid taken by mouth: **0.2 mg/kg** per day	**Fenfluramine** as a liquid taken by mouth: **0.2 mg/kg** for the first day, then slowly increased over 8 days to **0.8 mg/kg** per day
	2 doses each day for up to 16 weeks		

Participants in Part 1 of this study could move on to Part 2 if the study doctors thought they would benefit from long-term treatment with fenfluramine.

The chart below shows the treatment the researchers planned to study in **Part 2**:

	Fenfluramine
	**Cohort A:** 247 participants **Cohort B:** 32 participants
	**Fenfluramine** as a liquid taken by mouth: **0.2 mg/kg** at first, then slowly increased up to **0.8 mg/kg** per day if the study doctors thought a higher dose would help
	Up to 5 years

What happened during this study?

Each participant, or their parent or caregiver, learned about the study and decided to join the study or to let the participant join the study in a process called “informed consent”.

The chart below shows what happened in this study for each participant:

Before study treatment
1 site visit

The doctors:

- Checked the health of the participants to make sure they could stay in the study
- Did physical exams and asked about the participants’ medications and any medical problems
- Took blood and urine samples
- Checked the participants’ heart health

The participants or their caregivers:

- Filled out questionnaires about the participants’ quality of life
- Kept track of the participants’ seizures

Up to 4 weeks before starting treatment in Part 1

During study treatment
Part 1: 4 site visits and 5 phone visits
Part 2: 2 site visits or phone visits at least every 3 months

The doctors:

- Did a physical exam and asked about the participants’ medications and any medical problems
- Took blood and urine samples
- Checked the participants’ heart health

The participants or their caregivers:

- Filled out questionnaires about the participants’ quality of life
- Kept track of the participants’ seizures

The participants:

- Took their study treatment

Up to 16 weeks in Part 1, and up to 5 years in Part 2

After study treatment
1, 3, or 4 site visits

The doctors:

- Did physical exams and asked about the participants’ medications and any medical problems
- Took blood and urine samples
- Checked the participants’ heart health

The participants or their caregivers:

- Filled out questionnaires about the participants’ quality of life
- Kept track of the participants’ seizures

Up to 2 years after finishing study treatment

What were the results of the study?

This is a summary of the main results from this study. These are the results from all the participants combined. The individual results of each participant might be different and are not in this summary.

Deciding which treatments work best usually takes results from several studies. Other studies may provide new information or different results. Always talk to a doctor before making any treatment decisions.

Did fenfluramine help the participants have fewer seizures?

Yes. In Part 1 of this study, the participants in Cohort A who took 0.8 mg/kg per day of fenfluramine had fewer seizures than the participants in Cohort A who took the placebo. Cohort A included most of the participants in this study. The researchers also kept track of seizures in the participants in Cohort B, and the participants who took 0.2 mg/kg per day of fenfluramine. But this was not part of the main question researchers were interested in answering, so these results are not in this summary.

To answer this question, the researchers asked the participants or their caregivers to keep track of the participants' seizures in an electronic diary. The researchers were specifically interested in drop seizures, which are common in LGS. Using the results in the electronic diaries, the researchers calculated the average number of drop seizures that each participant had every 4 weeks. The researchers called this the **drop seizure frequency** (**DSF**).

Researchers wanted to learn whether the number of drop seizures the participants had changed over time. To keep track of this, the researchers calculated the percentage difference in the participants' DSF after taking fenfluramine or the placebo compared to before they joined the study. This is also called the percentage change from baseline.

The **percentage change from baseline** in the DSF helps researchers keep track of changes in the number of drop seizures participants have over time:

- If the percentage change from baseline is a **positive number**, it means that the number of drop seizures **increased** during the study.
- If the percentage change from baseline is a **negative number**, it means that the number of drop seizures **decreased** during the study.

Researchers compared the percentage change from baseline in the DSF between the participants who took 0.8 mg/kg per day of fenfluramine and the participants who took the placebo. To do this, they calculated the median percentage change from baseline for each group. The **median** is the middle number in a set of numbers when ordered from lowest to highest.

The median percentage change from baseline in the DSF for each group in Cohort A of Part 1 is shown below.

	Median percentage change from baseline in DSF
Placebo	-7.6%
0.8 mg/kg per day of fenfluramine	-26.5%

The researchers found that there was a significant difference between the group that took 0.8 mg/kg per day of fenfluramine and the group that took the placebo. For this reason, the researchers concluded that 0.8 mg/kg of fenfluramine decreased the number of drop seizures more than the placebo.

What medical problems did the study doctors report as possibly related to study treatment?

This section is a summary of the medical problems that the participants had during the study that the doctors reported as **possibly related** to study treatment. These medical problems are called "**adverse reactions**".

In Part 1 of the study, participants took either fenfluramine or the placebo, and in Part 2 of the study, all participants took fenfluramine.

In Part 1 of this study, the doctors did not know what the participants were taking when the medical problems happened. The study doctors reported the medical problems they thought were caused by their study drug, even though the participants could have taken the placebo. So, some adverse reactions may be reported in participants who took the placebo, even though the placebo does not directly cause medical problems.

Some participants had more than 1 adverse reaction. Seizures that got worse could be counted as adverse reactions if the study doctors thought they might have gotten worse due to study treatment.

This summary also includes information about serious adverse reactions. An adverse reaction is considered “serious” when it is life-threatening, causes lasting problems, or requires hospital care.

Other studies may or may not show that these medical problems were possibly related to study treatment. The results from several studies are often needed to decide if a treatment causes an adverse reaction. Always talk to a doctor before making any treatment decisions.

Did any adverse reactions happen during this study?

Part 1

There were 46.0% of participants (121 of 263) who had an adverse reaction in Cohort A, Part 1 of this study.

Adverse reactions in **Cohort A, Part 1**

	Placebo (out of 87 participants)	**0.2 mg/kg of fenfluramine** (out of 89 participants)	**0.8 mg/kg of fenfluramine** (out of 87 participants)
How many participants had **serious** adverse reactions?	none	1.1% (1 participant)	1.1% (1 participant)
How many participants had adverse reactions?	42.5% (37 participants)	40.4% (36 participants)	55.2% (48 participants)
How many participants left the study due to adverse reactions?	none	3.4% (3 participants)	5.7% (5 participants)

There were 51.5% of participants (17 of 33) who had an adverse reaction in Cohort B, Part 1 of this study.

Adverse reactions in **Cohort B, Part 1**

	Placebo (out of 11 participants)	**0.2 mg/kg of fenfluramine** (out of 11 participants)	**0.8 mg/kg of fenfluramine** (out of 11 participants)
How many participants had **serious** adverse reactions?	none	9.1% (1 participant)	none
How many participants had adverse reactions?	27.3% (3 participants)	63.6% (7 participants)	63.6% (7 participants)
How many participants left the study due to adverse reactions?	none	9.1% (1 participant)	none

Part 2

There were 42.9% of participants (106 of 247) who had an adverse reaction in Cohort A, Part 2 of this study.

Adverse reactions in **Cohort A, Part 2**

	Any dose of fenfluramine (out of 247 participants)
How many participants had **serious** adverse reactions?	4.9% (12 participants)
How many participants had adverse reactions?	42.9% (106 participants)
How many participants left the study due to adverse reactions?	4.9% (12 participants)

There were 65.6% of participants (21 of 32) who had an adverse reaction in Cohort B, Part 2 of this study.

Adverse reactions in **Cohort B, Part 2**

	Any dose of fenfluramine (out of 32 participants)
How many participants had **serious** adverse reactions?	3.1% (1 participant)
How many participants had adverse reactions?	65.6% (21 participants)
How many participants left the study due to adverse reactions?	6.3% (2 participants)

What serious adverse reactions did the participants have?

Part 1

The most common **serious** adverse reaction in Part 1 was feeling sleepy (Somnolence).

The tables below show the serious adverse reactions that happened during Part 1.

Serious adverse reactions in **Cohort A, Part 1**

Serious adverse reaction	**Placebo** (out of 87 participants)	**0.2 mg/kg of fenfluramine** (out of 89 participants)	**0.8 mg/kg of fenfluramine** (out of 87 participants)
Feeling sleepy (Somnolence)	none	none	1.1% (1 participant)
A change in seizure appearance	none	1.1% (1 participant)	none

Serious adverse reactions in **Cohort B, Part 1**

	Placebo (out of 11 participants)	**0.2 mg/kg of fenfluramine** (out of 11 participants)	**0.8 mg/kg of fenfluramine** (out of 11 participants)
Feeling sleepy (Somnolence)	none	9.1% (1 participant)	none

None of the participants in Part 1 died due to serious adverse reactions.

Part 2

The most common **serious** adverse reaction in Part 2 was a change in seizure appearance.

The tables below show the serious adverse reactions that happened during Part 2.

Serious adverse reactions in **Cohort A, Part 2**

Serious adverse reaction	**Any dose of fenfluramine** (out of 247 participants)
A change in seizure appearance	1.2% (3 participants)
Decreased appetite	0.8% (2 participants)
Feeling sleepy (Somnolence)	0.8% (2 participants)
A seizure, or back-to-back seizures, that lasted too long (Status epilepticus)	0.8% (2 participants)
Feeling weak or lacking energy (Asthenia)	0.4% (1 participant)
Decreased levels of a protein called albumin in the blood, which can be a sign of medical problems (Hypoalbuminemia)	0.4% (1 participant)
Weight loss	0.4% (1 participant)

Serious adverse reaction in **Cohort B, Part 2**	
Serious adverse reaction	**Any dose of fenfluramine** (out of 32 participants)
Feeling sleepy (Somnolence)	3.1% (1 participant)

None of the participants in Part 2 died due to serious adverse reactions.

What adverse reactions did the participants have?

Part 1

The most common adverse reaction in Part 1 was decreased appetite.

The table below shows the adverse reactions that happened in 5.0% or more of participants in any treatment group in **Cohort A, Part 1**. There were other adverse reactions, but those happened in fewer participants.

Adverse reactions in 5.0% or more of participants in any group of **Cohort A, Part 1**			
Adverse reaction	**Placebo** (out of 87 participants)	**0.2 mg/kg of fenfluramine** (out of 89 participants)	**0.8 mg/kg of fenfluramine** (out of 87 participants)
Decreased appetite	10.3% (9 participants)	14.6% (13 participants)	29.9% (26 participants)
Feeling tired (Fatigue)	8.0% (7 participants)	6.7% (6 participants)	17.2% (15 participants)
Feeling sleepy (Somnolence)	9.2% (8 participants)	9.0% (8 participants)	14.9% (13 participants)
Weight loss	2.3% (2 participants)	3.4% (3 participants)	6.9% (6 participants)
Low energy or tiredness (Lethargy)	2.3% (2 participants)	1.1% (1 participant)	5.7% (5 participants)
Seizure	1.1% (1 participant)	7.9% (7 participants)	4.6% (4 participants)

The table below shows the adverse reactions that happened in 2 or more participants in any treatment group in **Cohort B, Part 1**. There were other adverse reactions, but those happened in fewer participants.

Adverse reactions in 2 or more of participants in any group of **Cohort B, Part 1**

Adverse reaction	**Placebo** (out of 11 participants)	**0.2 mg/kg of fenfluramine** (out of 11 participants)	**0.8 mg/kg of fenfluramine** (out of 11 participants)
Feeling sleepy (Somnolence)	9.1% (1 participant)	36.4% (4 participants)	27.3% (3 participants)
Decreased appetite	18.2% (2 participants)	27.3% (3 participants)	27.3% (3 participants)
Weight loss	9.1% (1 participant)	18.2% (2 participants)	27.3% (3 participants)
Diarrhea	none	27.3% (3 participants)	18.2% (2 participants)

Part 2

The most common adverse reaction in Part 2 was decreased appetite.

The table below shows the adverse reactions that happened in 5.0% or more of participants in any treatment group in **Cohort A, Part 2**. There were other adverse reactions, but those happened in fewer participants.

Adverse reactions in 5.0% or more of participants in **Cohort A, Part 2**

Adverse reaction	**Any dose of fenfluramine** (out of 247 participants)
Decreased appetite	13.8% (34 participants)
Feeling tired (Fatigue)	8.5% (21 participants)
Feeling sleepy (Somnolence)	6.1% (15 participants)

The table below shows the adverse reactions that happened in 10.0% or more of participants in any treatment group in **Cohort B, Part 2**. There were other adverse reactions, but those happened in fewer participants.

Adverse reactions in 10.0% or more of participants in **Cohort B, Part 2**

Adverse reaction	**Any dose of fenfluramine** (out of 32 participants)
Feeling sleepy (Somnolence)	31.3% (10 participants)
Increased levels of the hormone prolactin in the blood, which can be a sign of medical problems	18.8% (6 participants)
Decreased appetite	12.5% (4 participants)
Weight loss	12.5% (4 participants)

What did the researchers learn from this study?

The results of this study have helped researchers learn more about using fenfluramine in people living with LGS. In this study, the researchers found that:

- Fenfluramine helped to reduce the number of drop seizures that participants had compared to the placebo.
- 46.6% of participants in both cohorts (138 of 296) had an adverse reaction in Part 1 of this study, and 45.5% of participants (127 of 279) had an adverse reaction in Part 2.
- The most common adverse reaction was decreased appetite.

Deciding which treatments work best for patients almost always takes results from several studies. This summary shows only the main results from this one study. Other studies may provide new information or different results.

The purpose of this summary is only to share information. If you need medical advice about your or your child's health or situation, please contact your doctor.

When this document was approved, further clinical studies with fenfluramine were ongoing.

Where can I learn more about this study?

You can find more information about this study at the websites listed below:

- www.clinicaltrials.gov/ct2/show/study/NCT03355209
- www.clinicaltrialsregister.eu/ctr-search/search?query=2017-002628-26

If you have questions about this study, UCB contact information is available at www.ucb.com/UCBcares.

Study Information

Protocol Number: ZX008-1601

National Clinical Trial Number: NCT03355209

EudraCT Number: 2017-002628-26

Study Sponsor: UCB Biopharma SRL sponsored this study. It is referred to as UCB in this summary.

Full Study Title: A Two-Part Study of ZX008 in Children and Adults with Lennox-Gastaut Syndrome (LGS); Part 1: A Randomized, Double-blind, Placebo-controlled Trial of Two Fixed Doses of ZX008 (Fenfluramine Hydrochloride) Oral Solution as Adjunctive Therapy for Seizures in Children and Adults with LGS, Followed by Part 2: An Open-label Extension to Assess Long-Term Safety of ZX008 in Children and Adults with LGS

Thank you

Participants in clinical studies belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

CISCRP REVIEW PANEL

This summary was last updated on 9 June 2025.
The final clinical study report is dated 28 November 2024.