# Plain Language Clinical Study
# Summary

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

**Sponsor:** Pfizer Inc.

**Medicine Studied:** Zavegepant

**Protocol Number:** C5301006 (BHV3500-302)

**Dates of Study:** 26 March 2021 to 21 March 2024

**Title of this Study:** A Study to Learn About the Effects and Safety of Oral Zavegepant to Prevent Migraine

[A Phase 2/3 Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Oral Zavegepant in Migraine Prevention]

**Date of this Report:** 20 March 2025

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# – Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. Do you have any questions about the study or the results? If so, please contact the doctor or staff at your study site.

# Why was this study done?

## What is migraine?

Migraine is a long-term (chronic) condition in which a person experiences a throbbing or pulsating headache usually on 1 side of the head. Other symptoms include nausea, vomiting, and sensitivity to light and sound. People may get repeated headaches, called attacks, which can last from 4 hours to 3 days. Migraine attacks may be triggered by stress, changes in sleep patterns, changes in the body's hormone levels or some other reasons. Migraines can significantly impact daily life, making it difficult to work, study, or enjoy normal activities. Migraine days is a term to describe the number of days in a calendar month when a person experiences a migraine headache.

## What is Zavegepant?

A protein called CGRP is released during migraine attacks. This protein attaches to the receptors (targets), cause nerve inflammation and increased pain signals to the brain. Zavegepant works by helping block CGRP receptors. This can treat and help to prevent migraine attacks.

In this study, zavegepant was used as oral capsules taken by mouth. Zavegepant as a nasal spray, known as ZavzPret is approved for a different indication.

## What was the purpose of this study?

The purpose of the study was to learn about the effect and safety of zavegepant, compared to "placebo" in the prevention of migraine. A placebo does not have any medicine in it, but it looks just like the study medicine.

The study stopped early because of business reasons after a change in the development plan for oral zavegepant. This was not due to any safety concern.

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### Researchers wanted to know:

**What was the average change in the number of migraine days in a month, for participants treated with zavegepant compared to placebo, over the 3-month treatment period?**

This study stopped early and was not completed as planned. The results shown below for the main research question are not meaningful. There is not enough information to reach a conclusion.

## What happened during the study?

### How was the study done?

Researchers tested zavegepant in a group of study participants to find out if the study participants taking zavegepant experienced a change in the number of migraine days during the first 3 months of treatment.

Researchers then compared the results of study participants taking the study medicine to the results of study participants taking a placebo.

The study had 3 periods: observation period, treatment period, and follow-up period as shown in figure 1.

**Observation Period:** For about a month, the researchers checked who could take part in this study. During this phase, participants were provided with an electronic diary (eDiary) to record occurrences of their migraine and the symptoms.

**Treatment Period:** The treatment period had 2 parts. In **Part 1**, the study participants and researchers did not know who took zavegepant and who took the placebo. This is known as a "blinded" study. In **Part 2**, both the researchers and the study participants knew which treatment was given. Throughout the study, the Sponsor knew the treatment being given.

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During Part 1, the participants were divided into 4 groups by chance alone. This is called randomization. Two groups took zavegepant as either zavegepant 100 mg or zavegepant 200 mg and the other 2 groups took placebo that looked like zavegepant 100 mg or zavegepant 200 mg.

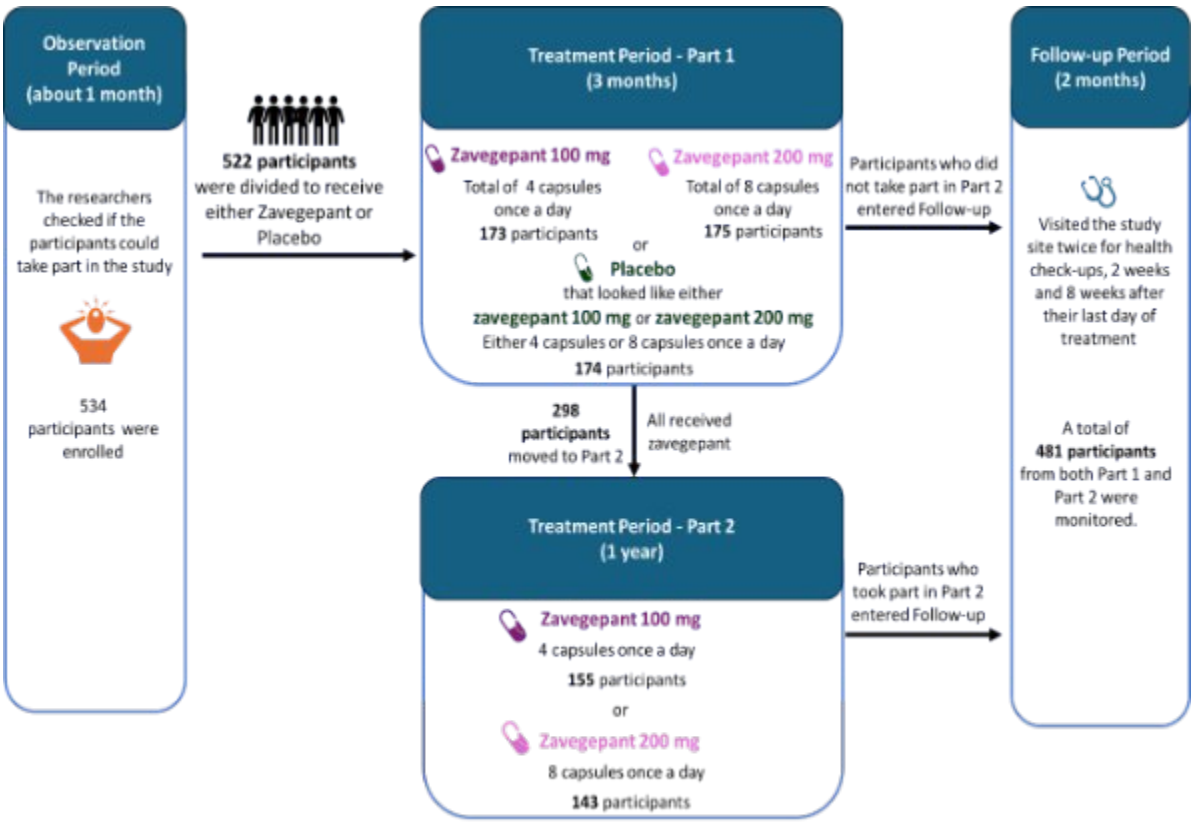
Part 1 was conducted for 3 months. The study participants recorded their migraine occurrence and symptoms in the eDiary during the treatment period. They also filled in forms with question on quality of life and if they took any medicines apart from the study drug.

On completion of Part 1, the participants moved to Part 2. All the participants in Part 2 took zavegepant 100 mg or zavegepant 200 mg. It was conducted for 1 year.

**Follow-up Period:** All participants visited the study site twice for health checks. Visits were 2 weeks and 8 weeks after their last day of treatment. Participants' health was monitored throughout the study.

The study stopped early due to business reasons after a change in the development plan for zavegepant. This was not due to any safety concern.

## Figure 1: What happened during the study




## Where did this study take place?

The Sponsor ran this study in the United States.

## When did this study take place?

It began 26 March 2021 and ended 21 March 2024.

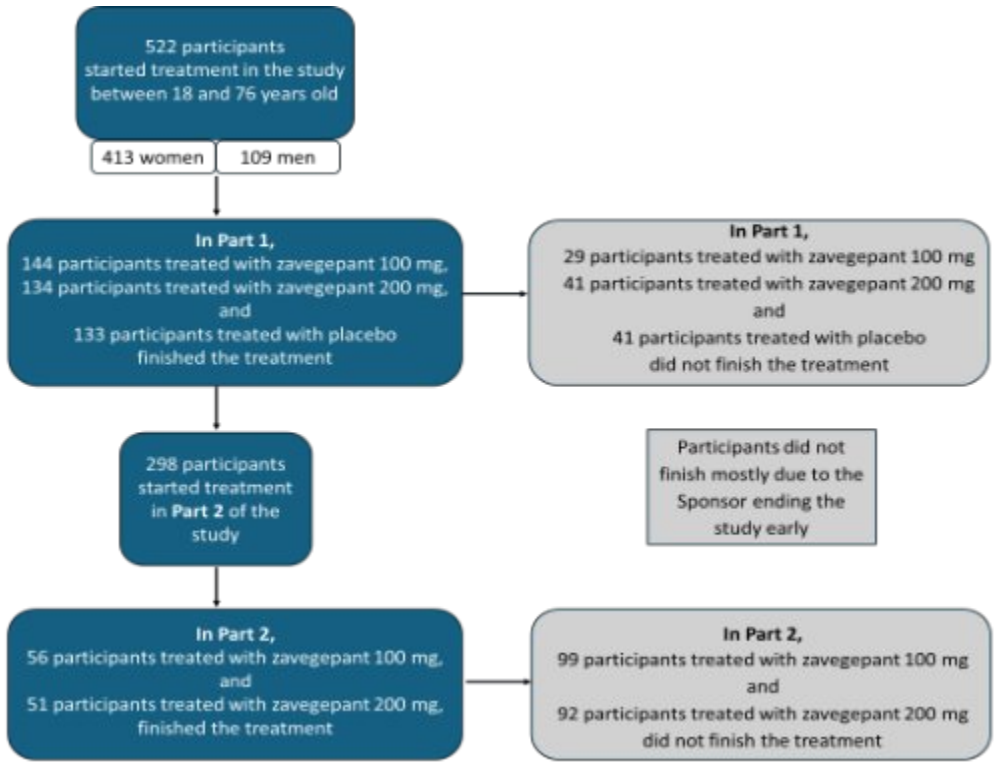
## Who participated in this study?

The study included participants who had chronic migraine for at least 1 year. They had 8 or more migraine days every month, and 15 or more "headache days" every month during the 3 months before the study started. Headache days are calendar days when a person experiences a headache that could be a migraine or a non-migraine headache.

Participants were to be treated until 3 months in Part 1 and for 1 year in Part 2.

Figure 2 below shows how many participants finished the treatment.

## Figure 2: How many participants finished the treatment




## How long did the study last?

Study participants were in the study for about 6 months during Part 1 and for a little more than 1 year during Part 2. The entire study took around 3 years before the Sponsors decided to stop the study. This decision was not due to any safety concerns with zavegepant.

When the study ended in March 2024, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

# What were the results of the study?

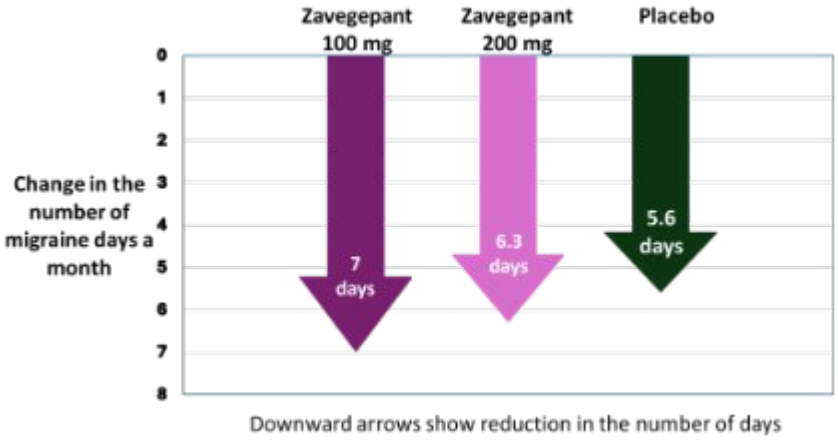
## What was the average change in the number of migraine days in a month, for participants treated with zavegepant compared to placebo, over the 3-month treatment period?

This study stopped early and was not completed as planned. The results shown below for the main research question are not meaningful. There is not enough information to reach a conclusion.

To answer this question, the researchers measured the change in the number of migraine days that each participant experienced in a month after 3 months of treatment during Part 1. The results from participants who took zavegepant were compared with those who took placebo.

## Did the study medicine help in reducing the number of migraine days in a month compared to placebo?

On average, participants who took zavegepant 100 mg had a reduction of 7 days, participants who took zavegepant 200 mg had a reduction of 6.3 days while participants who took placebo experienced a reduction of 5.6 days. All participants who received placebo were combined in a single group.




Downward arrows show reduction in the number of days

# What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medicine might have on a participant.

During **Part 1**, 63 out of 173 participants (36%) who took zavegepant 100 mg, 51 out of 175 participants (29%) who took zavegepant 200 mg and 61 out of 174 participants (35%) who took placebo in this study had at least 1 medical problem. A total of 2 participants in zavegepant 100 mg group, 5 participants in zavegepant 200 mg group and 7 participants in placebo group, left the study because of medical problems. The most common medical problems – those reported by 5 or more participants in any group – are described below in Table 1.

Below are instructions on how to read Table 1.

### Instructions for Understanding Table 1

- The first row of the table shows the groups in the study and the number of participants in each group.
- The grey and white rows in Table 1 show individual medical

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## Instructions for Understanding Table 1

- The first row of the table shows the groups in the study and the number of participants in each group.
- The grey and white rows in Table 1 show individual medical problems that were commonly reported by 5 or more participants.
- The **1st** column of Table 1 tells how many of the 173 participants who took zavegepant 100 mg reported each medical problem. Below the number is the percentage of the 173 participants who took zavegepant 100 mg and reported the medical problem.
- The **2nd** column of Table 1 tells how many of the 175 participants who took zavegepant 200 mg reported each medical problem. Below the number is the percentage of the 175 participants who took zavegepant 200 mg and reported the medical problem.
- The **3rd** column of Table 1 tells how many of the 174 participants who took placebo reported each medical problem. Below the number is the percentage of the 174 participants who took placebo and reported the medical problem.
- Using these instructions, you can see that 12 out of the 173 participants (7%) who took zavegepant 100 mg reported nausea. 5 out of the 175 participants (3%) who took zavegepant 200 mg reported nausea. A total of 13 out of the 174 participants (8%) who took a placebo reported nausea.

| Table 1. Commonly reported medical problems by study participants during Part 1 | | |
|---|---|---|
| **Zavegepant 100 mg (173 Participants)** | **Zavegepant 200 mg (175 Participants)** | **Placebo 100 mg (174 Participants)** |
| **Nausea** | | |
| 12 out of 173 participants (7%) | 5 out of 175 participants (3%) | 13 out of 174 participants (8%) |
| **COVID-19** | | |
| 8 out of 173 participants (5%) | 8 out of 175 participants (5%) | 3 out of 174 participants (2%) |
| **Inflammation of the nose and throat** | | |
| 5 out of 173 participants (3%) | 1 out of 175 participants (less than 1%) | 2 out of 174 participants (4%) |
| **Inflammation of the sinuses** | | |
| 3 out of 173 participants (2%) | 3 out of 173 participants (2%) | 3 out of 173 participants (2%) |
| **Infection of the parts of the body that collect and pass out urine** | | |
| 2 out of 173 participants (1%) | 1 out of 175 participants (less than 1%) | 7 out of 174 participants (4%) |
| **Diarrhea** | | |
| 1 out of 173 participants (less than 1%) | 2 out of 175 participants (1%) | 6 out of 174 participants (3%) |

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During **Part 2**, 66 out of 155 participants (43%) who took zavegepant 100 mg and 67 out of 143 participants (47%) who took zavegepant 200 mg in this study had at least 1 medical problem. A total of 2 participants in zavegepant 100 mg group and 4 participants in zavegepant 200 mg group, left the study because of medical problems. The most common medical problems – those reported by 5 or more participants in any group – are described below in Table 2.

Below are instructions on how to read Table 2.

**Instructions for Understanding Table 2.**

- The **1st** column of Table 2 lists medical problems that were commonly reported during the study. All medical problems reported by 5 or more participants are listed.
- The **2nd** column tells how many of the 155 participants who took zavegepant 100 mg reported each medical problem. Next to this number is the percentage of the 155 participants who took the zavegepant 100 mg and reported the medical problem.
- The **3rd** column tells how many of the 143 participants who took zavegepant 200 mg reported each medical problem. Next to this number is the percentage of the 143 participants who took zavegepant 200 mg and reported the medical problem.
- Using these instructions, you can see that 12 out of the 155 participants (8%) who took zavegepant 100 mg reported COVID-19. A total of 12 out of the 143 participants (8%) who took zavegepant 200 mg reported COVID-19.

**Table 2. Commonly reported medical problems by study**

| participants during Part 2 | | |
|---|---|---|
| **Medical Problem** | **Zavegepant 100 mg (155 Participants)** | **Zavegepant 200 mg (143 Participants)** |
| **COVID-19** | 12 out of 155 participants (8%) | 12 out of 143 participants (8%) |
| **Inflammation of the nose and throat** | 7 out of 155 participants (5%) | 4 out of 143 participants (3%) |
| **Infection of the parts of the body that collect and pass out urine** | 6 out of 155 participants (4%) | 2 out of 143 participants (1%) |
| **Increase in the blood level of a protein called creatine phosphokinase** | 5 out of 155 participants (3%) | 3 out of 143 participants (2%) |
| **Nose and throat infection** | 5 out of 155 participants (3%) | 2 out of 143 participants (1%) |
| **Nausea** | 3 out of 155 participants (2%) | 6 out of 143 participants (4%) |

# Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

During **Part 1**, 3 out of 522 participants (less than 1%) had serious medical problems.

- Two (2) participants in the zavegepant group had serious medical problems. One (1) participant had heart issues caused by high blood pressure in zavegepant 100 mg group and 1 participant had low levels of hemoglobin due to less iron in blood in zavegepant 200 mg group.
- One (1) participant in the placebo group had COVID-19.

During **Part 2**, 4 out of 298 participants (1%) had serious medical problems. All participants received zavegepant.

- In zavegepant 100 mg group, 1 participant had kidney stones.
- In zavegepant 200 mg group, 2 participants had inflammation of the gallbladder, 1 participant each had blockage in intestine and lung disorder.

One (1) participant died during the study. This was not related to treatment.

## Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results

Use the protocol number **C5301006 (BHV3500-302)**

The full scientific report of this study is available online at:

www.clinicaltrials.gov

Use the study identifier **NCT04804033**

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Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!

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