CLINICAL STUDY RESULTS

A Study to Estimate the Effect of Fluvoxamine and Paroxetine on the Level of IPN60170 (Mesdopetam) in the Blood of Healthy Volunteers

This study suggests that the levels of IPN60170 (Mesdopetam) in the blood can increase if given with medicines like fluvoxamine (CYP1A2 blocking agent), and does not change if given with medicines like paroxetine (CYP2D6 blocking agent).

The results shown in this summary are from one clinical study. Other clinical studies may produce different results.

This lay summary was created by Ipsen with the assistance of a third-party writing service provider.

What was the study about?

Mesdopetam was developed to treat a condition called levodopa-induced dyskinesia (LID) in patients with Parkinson's disease (PD).

PD happens due to a lack of a chemical called dopamine in the brain, causing strong body shaking, stiffness, and problems with balance, coordination, and walking. Levodopa is a drug used to treat PD patients. However, it causes side effects like involuntary and erratic movements of the face, arms, legs, or trunk called LID.

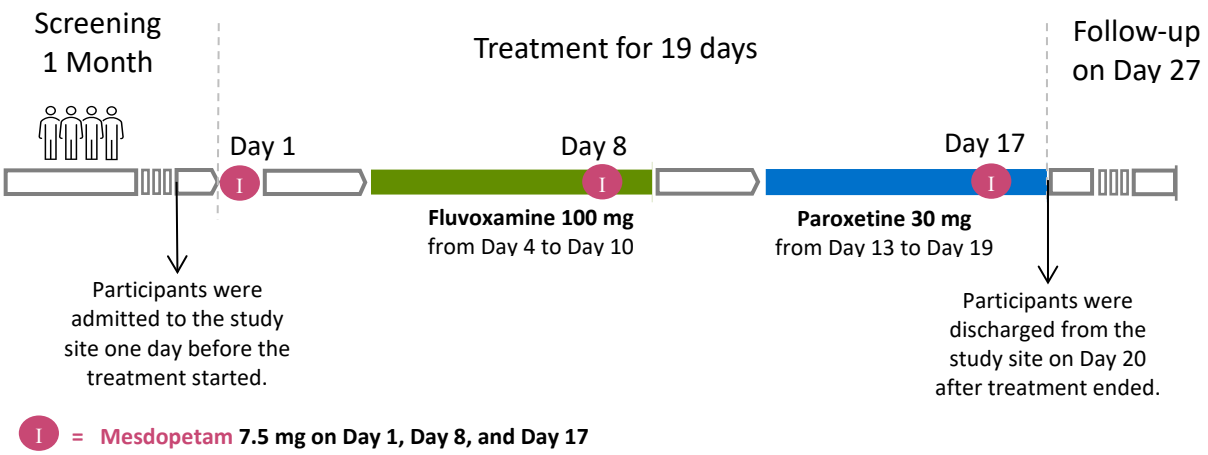
Mesdopetam is a drug that is being developed for the treatment of LID. To ensure mesdopetam is safe and effective, researchers wanted to know how the amount of mesdopetam in the blood changes when this was taken with fluvoxamine or with paroxetine.

Fluvoxamine and paroxetine are drugs already available on the market that are known to block proteins in the liver called CYP1A2 and CYP2D6, respectively. These proteins are involved in the break-down of mesdopetam in the body. M1 is one of the breakdown products of mesdopetam which can be formed via CYP1A2 and CYP2D6. Taking either fluvoxamine or paroxetine with mesdopetam may slow down the breakdown of mesdopetam to M1 in the body. If mesdopetam is not broken down, it may accumulate in the body and potentially cause harmful effects.

The aim of this study was to estimate the effect of fluvoxamine or paroxetine on the blood levels of mesdopetam and its breakdown product (M1) in healthy male volunteers.

The study took place between April and October 2022 at one study site in the United States of America. Another stage, investigating the effect of smoking (CYP1A2 activating agent) on the level of mesdopetam in the blood, was planned for this study but was not conducted as the sponsor decided to close the study.

Participants and the study team knew what treatments were being given. This is known as an “open-label” study.



Screening: The study doctor checked if participants could take part in this study.

Treatment: Eligible participants stayed in the study site for 21 days and received the following treatments:

- On Day 1, participants received a single 7.5 mg dose of mesdopetam.
- From Day 4 to Day 10, participants received fluvoxamine 100 mg once daily, and on Day 8, they received a single 7.5 mg dose of mesdopetam along with fluvoxamine.
- From Day 13 to Day 19, participants received paroxetine 30 mg once daily, and on Day 17, they received a single 7.5 mg dose of mesdopetam along with paroxetine.

Participants received these treatments on an empty stomach.

The participants' health was monitored throughout the study. Blood samples were collected at defined timepoints over 4 days after each mesdopetam administration to measure the level of mesdopetam and its breakdown product (M1).

Follow-up: Participants returned to the study site on Day 27 to confirm their overall health and wellbeing.

Who took part in this study?

20 HEALTHY MALE VOLUNTEERS

36 YEARS AVERAGE AGE

Participants were eligible to take part in the study if they:

- were healthy males,
- were adults aged between 25 and 55 years weighing 50 kg or more,
- had normal functioning CYP1A2 and CYP2D6 liver proteins, and
- had no history of smoking cigarettes 6 months before the start of the study.

Participants were not eligible to take part in the study if they:

- had any medical condition that put their health or life at risk, as per the study doctor,
- had any surgery, had a medical condition, or were taking medicines that could interfere with the study results,
- had a history of abuse, dependence, or addiction to alcohol or a drug 6 months before the start of the study, or
- had experienced harmful effects after taking fluvoxamine or paroxetine in the past.

What treatments were used?

Mesdopetam (Study Treatment)	Fluvoxamine	Paroxetine
Single dose of 7.5 mg capsule on Day 1, Day 8, and Day 17 by mouth	100 mg tablet daily for 1 week from Day 4 to Day 10 by mouth	30 mg tablet daily for 1 week from Day 13 to Day 19 by mouth

What did researchers find in the study?

Researchers found out that blood levels of mesdopetam increased when given with fluvoxamine (CYP1A2 blocking agent) but did not change when given with paroxetine (CYP2D6 blocking agent).

What was the effect of fluvoxamine and paroxetine on the blood levels of mesdopetam and its breakdown product (M1), in healthy male participants?

To answer this question, study doctors measured the blood levels of mesdopetam and M1 when mesdopetam was given with fluvoxamine or paroxetine and compared them with the blood levels when mesdopetam was given alone.

The total amount and highest level of mesdopetam in the blood increased when mesdopetam was given with fluvoxamine, compared to when mesdopetam was given alone, whereas the total amount and highest level of M1 in the blood decreased.

However, the total amount and highest level of mesdopetam and M1 in the blood stayed nearly the same when mesdopetam was given alone or with paroxetine.

How did the treatment make participants feel?

During clinical studies, participants are asked to report if they feel unwell, experience any kind of medical event, or notice anything different about their bodies. These are called ‘adverse events.’ Researchers record all adverse events reported by participants, whatever the cause.

If the study doctor thinks an adverse event may be related to the study treatment, it is called a ‘side effect’ or a ‘treatment-related adverse event’. An adverse event or side effect is considered ‘serious’ when it is life-threatening, causes lasting problems, or leads to hospitalisation.

- Adverse events that are *life-threatening*, cause lasting problems or require an individual to go to the *hospital* are considered s*erious*.
- No participants in this study experienced serious side effects.
- No participants died during the study.

Overall, 4 out of 20 participants (20%) experienced the following side effects:

- **1 out of 20 participants (5%)** experienced a **headache** caused by **mesdopetam**.
- **3 out of 20 participants (15%)**, one each, experienced **diarrhea, vomiting, and difficulty concentrating** caused by **fluvoxamine**.
- **No participants experienced side effects** caused by **paroxetine**.

No participant stopped the study drug due to a side effect during the study.

More information

For more information about current treatments available, please speak to your healthcare provider. If you have any questions about this study, please contact the sponsor, Ipsen at:

clinical.trials@ipsen.com

Future research

There is no future research planned on this topic.

Study identification and other information

FULL STUDY TITLE: A Phase I, Single Group Treatment, Open-Label, Two-Stage Study to Investigate the Effect of Repeat Doses of Fluvoxamine (A Strong CYP1A2 Inhibitor) and Paroxetine (A Strong CYP2D6 Inhibitor) and Smoking on the Pharmacokinetics of Single-Dose IPN60170 in Healthy Male Participants.

PROTOCOL: CLIN-60170-450.

OTHER INFORMATION: Phase I studies can take several months to years to complete and look at how safe a potential new treatment is.

We thank all the volunteers who took part in this study. Without their support, advances in treatments for medical conditions would not be possible.

We would also like to thank the people who took the time to review this document to make it easier for a general audience to read.