An open label, randomized, 4 treatments, 4 periods, 4 sequence crossover study to assess the pharmacokinetics of four 6 g single-doses of once-nightly sodium oxybate (FT218) formulations with varying release rates in healthy volunteers

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The purpose of this study is to investigate how quickly and to what extent 4 different formulations of FT218 are absorbed, distributed, metabolized and eliminated from the body.It will also be investigated how safe FT218 is and how well it is...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Sleep disturbances (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON48344

Source
ToetsingOnline

Brief title
PKFT218-1902 4 way cross-over bioequivalence study

Condition

- Sleep disturbances (incl subtypes)

Synonym
Narcolepsy

Research involving
Human

Sponsors and support

Primary sponsor: Flamel Ireland Ltd doing business as Avadel Ireland
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: bioequivalence, cross-over, PKFT218

Outcome measures

Primary outcome

To assess bioequivalence of pharmacokinetic parameters Cmax, AUC0-t, and

AUC0-inf for sodium oxybate in plasma

Secondary outcome

Clinical and laboratory safety and tolerability. Safety will be evaluated based

on reported adverse events, physical examinations, pulse oximetry, vital signs,

ECG, and safety laboratory test results.

Study description

Background summary

FT218 is a new compound that may eventually be used for the treatment of narcolepsy. For some people with narcolepsy, it also involves a sudden loss of muscle tone (cataplexy), usually triggered by strong emotion. FT218 is a new formulation of the drug sodium oxybate/GHB, a substance that has depressant or sedating effects in people.

Sodium oxybate is a registered drug under the tradename Xyrem®. Xyrem® is an oral solution that has to be taken at bedtime, and then again 2.5 to 4 hours later. This dosing schedule is considered inconvenient for the patients because they have to wake up in the middle of the night to take the second dose. FT218 contains the same active substance (sodium oxybate) as Xyrem®, but in a special formulation which provides slower and longer release of the active substance.

As a result, FT218 only has to be taken once at bedtime. FT218 is in development and is not registered as a drug, but it has been given to over 300 humans before.

FT218 is made of the active ingredient sodium oxybate encapsulated in very small particles made of naturally occurring substances (polymers). The Sponsor has conducted research and studies to show that the particles used can be broken down by the human body and that the components are not harmful. These particles have been used previously in humans without any safety concern.

Study objective

The purpose of this study is to investigate how quickly and to what extent 4 different formulations of FT218 are absorbed, distributed, metabolized and eliminated from the body.

It will also be investigated how safe FT218 is and how well it is tolerated.

Study design

The actual study will consist of 4 periods during each of which the volunteer will stay in the research center for 2 days (1 night). In each treatment period, Day 1 is the day of administration of the study compound. In each treatment period, the volunteer is expected at the research center at 10:00 h in the morning of Day 1. In each treatment period, the volunteer will leave the research center on Day 2.

The study consists of 4 treatment periods. In each treatment period, the volunteer will receive a single dose of 6 gram of FT218 as an oral drink of 50 milliliters. After each administration of the study compound, the dosing cup will be rinsed once with 20 mL of water, which the volunteer will also be required to drink.

There are 4 different types of the FT218 drink: Types A, B, C and D. These 4 drinks all contain 6 g of FT218 but differ slightly in their composition.

Intervention

The study consists of 4 treatment periods. In each treatment period, the volunteer will receive a single dose of 6 gram of FT218 as an oral drink of 50 milliliters. After each administration of the study compound, the dosing cup will be rinsed once with 20 mL of water, which the volunteer will also be required to drink.

There are 4 different types of the FT218 drink: Types A, B, C and D. These 4

drinks all contain 6 g of FT218 but differ slightly in their composition.

Study burden and risks

In previous studies, FT218 was investigated in 172 healthy volunteers as single doses of 4.5 g, 6 g, and 7.5 g. The following is a list of side effects that were reported during these studies:

Very common (>10% of volunteers): nausea, sleepiness, dizziness, headache

Common (5-10% of volunteers): Feeling drunk, vomiting, somnolence, tiredness, abdominal discomfort, lightheaded feeling, drowsiness.

Uncommon (1-5% of volunteers): vertigo, pain and/or bruising at site of blood draw, fatigue, muscle relaxation, ataxia, feeling warm, insomnia, loose stool, neck and/or leg myalgia, increased sweating, decreased appetite, blurred vision, abnormal dreams, paresthesia, relaxed feeling, disturbed sleep, dyspnea (shortness of breath), numbness, common cold, dry mouth, feeling high, malaise, sedation, feeling worried

The active substance in FT218 (sodium oxybate) is the same as the active substance in Xyrem®, a registered drug. The risks associated with FT218 are expected to be similar to those associated with Xyrem®. As FT218 is a new once-nightly formulation of sodium oxybate, there may be some side effects that are not yet known. The following is a list of the known potential side effects of sodium oxybate:

The most commonly reported adverse reactions are dizziness, nausea, and headache, all occurring in 10% to 20% of patients.

Less common side effects (in 1% to 10% of patients) are nasopharyngitis, sinusitis, anorexia, decreased appetite, depression, cataplexy, anxiety, abnormal dreams, confused state, disorientation, nightmares, sleepwalking, sleep disorder, insomnia, insomnia in the middle of the night, nervousness, sleep paralysis, somnolence, tremor, balance disorder, disturbance in attention, hypoesthesia, paresthesia, sedation, dysgeusia, blurred vision, vertigo, palpitations, hypertension, dyspnea, snoring, nasal congestion, vomiting, diarrhea, upper abdominal pain, hyperhidrosis (increased sweating), rash, arthralgia, muscle spasms, back pain, enuresis nocturna, urinary incontinence, asthenia, fatigue, feeling drunk, edema peripheral, increased blood pressure, decreased weight, and risk of a fall.

Uncommon side effects (in 0.1% to 1% of patients) are hypersensitivity, suicide attempt, psychosis, paranoia, hallucination, abnormal thinking, agitation, initial insomnia, myoclonus, amnesia, restless leg syndrome, and fecal incontinence.

The most serious (but uncommon) adverse reactions are suicidal attempt, psychosis, respiratory depression and convulsion.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Gender: male or female; females may be of childbearing potential, of non-childbearing
potential, or postmenopausal.
2. Age: 18-65 years, inclusive, at screening
3. BMI: 18.0-30.0 kg/m2, inclusive, at screening
4. Weight: >=60 kg
5. Status: healthy, as determined by the Investigator. Determination will be based on full medical evaluation including past medical history, physical

examination, vital signs,laboratory tests, and ECG.

Exclusion criteria

1. The presence of any unstable or clinically significant medical or psychiatric disorders (asdetermined by medical or psychiatric history, physical examination, and/or clinical laboratory test) which in the opinion of the Investigator may either put the subject at risk by participation in the study or may influence the results of the study
2. History of seizures
3. Any finding in the medical history, physical examination, or clinical laboratory tests giving reasonable suspicion of a disease that would contraindicate taking FT218, or a known poor tolerability to the active compound
4. Subjects with a previous history or current ideation of suicide attempt
5. Subjects with a medical diagnosis of Major Depression, as defined by the DSM-IV Criteria for Major Depression Disorder, which in the opinion of the Investigator would impact subject safety and place the subject at risk by participation in the study

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-12-2019
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO Date:	27-11-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-12-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2019-004009-28-NL
CCMO	NL72100.056.19