A comparative, open-label, randomized, 2-stage sequential design, 2 periods, crossover study to demonstrate the bioequivalence of 2 FT218 batches (single dose of 4.5 gram) in healthy volunteers

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

Summary

ID

NL-OMON44364

Source
ToetsingOnline

Brief title
FT218 two batches bioequivalence study

Condition

- Sleep disturbances (incl subtypes)

Synonym
Narcolepsy, sleep / wake disorder

Research involving

Human

Sponsors and support

Primary sponsor: Flamel Ireland Limited (Ltd) trading under the business name Avadel Ireland
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Bioequivalence, FT218

Outcome measures

Primary outcome

To demonstrate the bioequivalence (BE) of the 2 different batches of FT218 at

the dose of 4.5 g

Secondary outcome

To assess the safety and tolerability of the 2 different batches of FT218 taken

2 hours post-evening meal at the dose of 4.5 g in healthy volunteers

Study description

Background summary

FT218 is a new formulation (composition) of the registered drug sodium oxybate. Sodium oxybate (also known as the sodium salt of gamma-hydroxybutyric acid [GHB]) is registered under the name Xyrem® for the treatment of narcolepsy. Narcolepsy is a sleeping disorder that involves excessive daytime sleepiness. For some people with narcolepsy it also involves a sudden loss of muscle tone (cataplexy), usually triggered by strong emotion. Sodium oxybate/GHB is a substance that has depressant or sedating effects in people. 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 molecule or 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 humans

before.

FT218 is made of the active ingredient sodium oxybate encapsulated in very small particles made of naturally occurring substances (polymers). Flamel has conducted all research and studies needed 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 the study is to investigate how quickly and to what extent 2 different production batches of FT218 (batch A and batch B) are absorbed and eliminated from the body (this is called pharmacokinetics). In this study it is investigated whether these characteristics are the same for both batches (this is also called bioequivalence). It will also be investigated to what extent FT218 is tolerated.

Study design

The actual study will consist of 2 periods during which the volunteer will stay in the clinical research center in Groningen (location Martini Hospital) for 2 days (1 night) during each period. The time interval between the 2 periods is at least 3 days.

Day 1 of each period is the day of administration of the study compound. In each period, the volunteer is expected at the clinical research center at 10:00 AM in the morning of Day 1. The volunteer will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water). The volunteer will leave the clinical research center in the afternoon of Day 2.

The post-study visit will take place 2 - 4 days after the volunteer has received the last dose of FT218. The appointment for the post-study visit will be made with the volunteer during the study.

The participation in the entire study, from the pre-study screening until the post study visit, will be approximately 4.5 weeks.

During the study the volunteer will receive FT218 in each period in the evening (around 22:00 h) of Day 1, 2 hours after completion of a standard dinner, as an oral drink (a suspension) of 50 milliliters. After administration of the study compound, the dosing cup will be rinsed once with 20 milliliters of water, which the volunteer will also be required to drink.

Intervention

The study will consist of 2 study periods during which the volunteer will receive a 4.5 grams dose of FT218 once in each study period. FT218 will be given as an oral drink (a suspension) of approximately 50 milliliters. The volunteer will receive one dose from each batch over the two periods. The order in which the volunteer will receive both batches will be determined by chance. The dose level of 4.5 grams matches one of the authorized nightly dose levels of Xyrem®.

Please refer to the table below to see the planned dose levels for the groups. Should, in the opinion of the investigators, unacceptable adverse effects appear, the study will be discontinued

The planning of the study is as follows:

Period Day Treatment How often
1 1 4.5 grams FT218 Once
2 1 4.5 grams FT218 Once

Study burden and risks

All drugs have the potential to cause adverse events. The active substance in FT218 is the same as the active substance in Xyrem® (sodium oxybate). The risks associated with FT218 are expected to be similar to those associated with Xyrem®.

In a previous study, FT218 was investigated in 40 healthy volunteers as single doses of 4.5 grams, 6 grams and 7.5 grams. In this study, Xyrem® was also administered, as well as other FT218 oral drinks with a slightly different composition than the drink used in this study. All tested FT218 formulations were well tolerated. Adverse events that were observed after FT218 administration were similar as after Xyrem® administration.

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 (common cold), sinusitis (sinus infection), anorexia, decreased appetite, depression, cataplexy (muscle weakness), anxiety (feeling of worry), abnormal dreams, confused state, disorientation (loss of sense of direction, position), nightmares, sleepwalking, sleep disorder, insomnia, insomnia in the middle of the night, nervousness, sleep paralysis (not able to move when falling asleep or at awakening), somnolence (sleepiness), tremor (muscle twitching), balance disorder, disturbance in attention (not being able to concentrate), hypoesthesia (reduced sense of touch), paresthesia (sensation of *pins and needles*), sedation (reduced state of awareness), dysgeusia (bad taste in the

mouth), blurred vision, vertigo (feeling of spinning), palpitations (rapid or irregular heartbeat), hypertension (high blood pressure), dyspnea (shortness of breath), snoring, nasal congestion, vomiting, diarrhea, upper abdominal pain, hyperhidrosis (increased sweating), rash, arthralgia (joint pain), muscle spasms, back pain, enuresis nocturna (bedwetting), urinary incontinence, asthenia (lack of energy), fatigue, feeling drunk, edema peripheral (swelling due to fluid retention), increased blood pressure, decreased weight, and risk of a fall.

Uncommon side effects in 0.1% to 1% of patients) include hypersensitivity, suicide attempt, psychosis (loss of contact with reality), hallucination (seeing or hearing things that are not real), abnormal thinking, agitation, initial insomnia (trouble falling asleep), myoclonus (muscle twitches), amnesia (memory loss), restless leg syndrome, and fecal incontinence.

Side effects for which frequency is not known are dehydration, suicidal ideation, euphoric mood, convulsion (abnormal, involuntary contraction of the muscles), respiratory depression (reduced urge to breathe), sleep apnea (pauses in breathing or shallow breaths while you sleep), dry mouth, urticaria (hives), and angioedema (swelling).

The most serious (but uncommon) adverse reactions are suicidal attempt, psychosis (loss of contact with reality), respiratory depression (reduced urge to breathe) and convulsion (abnormal, involuntary contraction of the muscles).

As with taking any drug, there is a risk of allergic reaction. Some symptoms of allergic reactions are: rash, difficulty breathing, and wheezing, sudden drop in blood pressure, a fast heart rate sweating, and swelling around the mouth, throat or eyes.

Procedures: pain, minor bleeding, bruising, possible infection

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

Gender: healthy male or female
Age: 18-65 years, inclusive, at screening
BMI: 18.0-28.0 kg/m2, inclusive
Weight: >=60 kg

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study. Donation or loss of more than 100 mL of blood within 60 days prior to the first drug administration. Donation or loss of more than 1.5 liters of blood (for men) / more than 1.0 liters of blood (for women) in the 10 months prior to the first drug
administration in the current 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):	07-08-2017
Enrollment:	62
Type:	Actual

Ethics review

Approved WMO

Date:	06-06-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	27-07-2017
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	EUCTR2017-000954-20-NL
CCMO	NL62068.056.17