# An exploratory, open-label, randomized, 2 treatments, 2 periods, 2 sequences crossover study to assess the pharmacokinetics of two FT218 batches (single dose administered at the dose of 6g) in healthy volunteers

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FT218 is a new formulation of the drug sodium oxybate (also known as the sodium salt of gamma-hydroxybutyric acid [GHB]), a registered drug under the tradename Xyrem® for the treatment of narcolepsy. FT218 has been administered to humans before.The...

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

## Summary

### ID

NL-OMON45837

**Source**
ToetsingOnline

**Brief title**
Exploratory PK study for FT218

### Condition

- Sleep disturbances (incl subtypes)

**Synonym**
Narcolepsy, sleep / wake disorder

**Research involving**

Human

## Sponsors and support

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

## Intervention

**Keyword:** FT218, PK

## Outcome measures

### Primary outcome

Plasma PK parameters of gamma-hydroxybutyric acid (GHB) estimated using

noncompartmental analysis, as appropriate: Cmax, tmax, kel, t1/2, AUC0-8h,

AUC0-t, AUC0-inf, AUC%extra, C8h.

### Secondary outcome

Adverse events, physical examinations, vital signs, pulse oximetry, 12-lead

electrocardiogram, and clinical laboratory tests.

# Study description

### Background summary

FT218 is a new compound that may eventually be used 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. 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 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 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**

FT218 is a new formulation of the drug sodium oxybate (also known as the sodium salt of gamma-hydroxybutyric acid [GHB]), a registered drug under the tradename Xyrem® for the treatment of narcolepsy. FT218 has been administered to humans before.

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. It will also be investigated how safe FT218 is and how well it is tolerated (i.e., possible side effects). In addition, the effect of FT218 on sleep efficiency and quality will be explored. The volunteer will receive both batches of FT218 once each. For this, the volunteer will stay 2 times in the research center.

**Study design**

The actual study will consist of 2 periods during which the volunteer will stay in the research center at the Martini Hospital location in Groningen. Each period will be 3 days (2 nights). 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 FT218. For both periods, the volunteer is expected at the research center at 14:00 h in the afternoon prior to the day of administration (so on Day -1). The volunteer will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the research center (with the exception of water). He/she will leave the research center in the afternoon of Day 2.

During the study, the volunteer will receive 6 gram (g) of FT218 twice (once from Batch A and once from Batch B). The order in which the volunteer will receive both batches will be determined by chance.

Administration of the study compound will occur in the evening (around 22:00 h), 2 hours after completion of a standardized dinner, as an oral drink (a suspension) of 50 milliliters (mL). After administration of the study compound,

the dosing cup will be rinsed once with 20 mL of water, which the volunteer is also be required to drink.

Please refer to the table below to see the planned dose levels. The study will be discontinued if, in the opinion of the investigators, unacceptable side effects appear.

Period Day Treatment Dose How often
1 1 Drink with FT218 Batch A or Batch B 6 grams Once
2 1 Drink with FT218 Batch A or Batch B 6 grams Once

**Intervention**

During the study, the volunteer will receive 6 gram (g) of FT218 twice (once from Batch A and once from Batch B). The order in which the volunteer will receive both batches will be determined by chance.

Administration of the study compound will occur in the evening (around 22:00 h), 2 hours after completion of a standardized dinner, as an oral drink (a suspension) of 50 milliliters (mL). After administration of the study compound, the dosing cup will be rinsed once with 20 mL of water, which the volunteer is also be required to drink.

**Study burden and risks**

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®.

FT218 has so far been administered to humans in multiple studies. The following side effects are most frequently observed: abdominal pain, nausea, dizziness and headache. Rarely occurring but important effects to mention are vomiting and respiratory depression. Because of the latter, you will be intensively monitored during the first 6 hours after administration of the study compound.

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. During your stay in the research center, you will be monitored continuously for any symptoms of an allergic reaction.

The study compound may also have side effects that are still unknown. As information becomes available, the volunteers will be informed about any changes in the way the study will be done and about any newly identified risks to which the volunteers may be exposed that may affect theirwillingness to participate in the study.

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 the current FT218 oral drink, and other FT218 oral drinks with a slightly different composition than the drink used in this study. All tested FT218 oral drinks were well tolerated. Adverse events that were observed after FT218 administration were similar as after Xyrem® administration. The reported side effects in this previous study included upper abdominal pain, nausea, stuffy nose, dizziness, joint pain and sore throat. All of these side effects were reported as being either mild or moderate and these side effects resolved quickly without any long-term effects noted.

In another study of FT218, single doses of 4.5 grams, 7.5 grams and 9 grams FT218 were studied in 20 healthy volunteers. In this study, the doses of 4.5 grams and 7.5 grams were well tolerated and reported adverse events were consistent with what was observed in the earlier study. Following administration of the highest dose level of 9 grams (1.5 times as high as the dose level that will be given in the current study), significant adverse events were reported in 2 out of the 12 volunteers who received this dose. A serious, but transient adverse effect occurred in 1 of the 12 volunteers who experienced deep sedation (loss of consciousness) with vomiting, necessitating hospitalization. After admittance to the hospital, the volunteer recovered fully within a few hours. A second volunteer experienced deep sedation but was aroused following stimulation at the time the event was noted by the clinical staff. Both volunteers made a full recovery with no lasting consequences.

In a third study, 22 additional healthy volunteers received 2 doses of 4.5 g FT218 without any safety concern. The 3 most recent studies, including 68 healthy volunteers receiving 2 doses of 6.0 g FT218 (or Xyrem®), also provided no new safety information.

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), paranoia, hallucination (seeing or hearing things that are not real), abnormal thinking, agitation, initial insomnia (trouble falling asleep), myoclonus (muscle twitches), amnesia (memory loss /memory impairment), restless leg syndrome, and fecal incontinence.

Side effects for which frequency is not known are dehydration, suicidal ideation, euphoric mood, homicidal ideation, aggression, sleep-related eating disorder, panic attack, mania / bipolar disorder, delusion, bruxism (teeth grinding), irritability, convulsion (abnormal, involuntary contraction of the muscles), loss of consciousness, dyskinesia (involuntary repetitive movements), tinnitus (ringing or buzzing in the ears), respiratory depression (reduced urge to breathe), sleep apnea (pauses in breathing or shallow breaths while you sleep), dry mouth, urticaria (hives), angioedema (swelling), pain in extremity, nocturia (excessive nighttime urination), pollakiuria (abnormally frequent urination) / micturition urgency, and hangover.

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).

Procedures: pain, minor bleeding, bruising, possible infection

# Contacts

**Public**
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**Scientific**
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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

- healthy male and female subjects
- 20-50 yrs, inclusive
- BMI: 18.0-28.0 kg / m2, inclusive

## 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 study 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 study drug administration

# Study design

## Design

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

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| Primary purpose: | Treatment |

### Recruitment

NL

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| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 11-10-2018 |
| Enrollment: | 20 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 17-09-2018 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 28-09-2018 |
| 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 | EUCTR2018-003060-32-NL |
| CCMO | NL67363.056.18 |