# A phase 1, randomized, double-blind, placebo-controlled study evaluating the pharmacokinetics of capsule and tablet formulations of VX-150, including the effects of food and milk, the relative bioavailability of the tablet formulation, and the drug-drug interaction between VX-150 and Midazolam, in healthy adults

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| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON45544

**Source**
ToetsingOnline

**Brief title**
A study to evaluate pharmacokinetics of VX-150 in healthy adults

### Condition

- Other condition

**Synonym**
pain

**Health condition**

pijn

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Vertex Pharmaceuticals Incorporated
**Source(s) of monetary or material Support:** Farmaceutische industrie

## Intervention

**Keyword:** Midazolam, pain, VX-150

## Outcome measures

**Primary outcome**

Plasma PK parameter estimates of VRT-1207355 and M5

**Secondary outcome**

- Plasma PK parameter estimates of midazolam and 1-hydroxy midazolam

- Safety and tolerability based on the incidence and type of AEs, changes from baseline in clinically significant laboratory test results, ECGs (standard and continuous), and vital signs at designated visits

# Study description

**Background summary**

VX 150 (also called study compound) is a new investigational drug. Investigational means the study compound is not approved for use and is still being tested for safety and effectiveness. This study compound may eventually be used for the treatment of pain. VX 150 is a blocker of sodium channels (Nav), specifically the NaV1.8 channel. Sodium channels are channels present in

the outer layer of cells, which allow sodium ions to enter the cell in certain circumstances. The NaV1.8 channel is primarily present in neurons that sense pain and it plays an important role in pain signaling.

**Study objective**

The purpose of Part A of the study is to investigate to what extent VX-150 is tolerated when administered as a single dose (capsule). The effect of taking the dose with food and milk on how quickly and to what extent VX-150 is absorbed, distributed, broken down and eliminated from the body will be investigated (this is called pharmacokinetics).

The purpose of Part B of the study is to investigate on how quickly and to what extent VX-150 is absorbed, distributed, broken down and eliminated from the body when administered for 11 or 14 days (capsule). In addition, the interaction between VX-150 or placebo in combination with midazolam will be investigated. Midazolam is a Food and Drug Administration (FDA)-approved, commercially available short acting sedative used prior to diagnostic or surgical procedures.

The purpose of Part C of the study is to investigate to what extent VX-150 is tolerated when administered as a single dose (tablet and capsule). The effect of taking the dose with food and milk on how quickly and to what extent VX-150 is absorbed, distributed, broken down and eliminated from the body will be investigated.

**Study design**

Part A:
The actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen (Location UMCG) for 20 days (19 nights).

The volunteer will receive VX-150 twice under fasted conditions, once under fed conditions and once with milk, as a capsule with 240 milliliters of (tap) water.

Part B:
For Group 1, the actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen (Location UMCG) for 14 days (13 nights).

The volunteer will receive the study compound (midazolam, VX-150 or placebo) under fed conditions, as a capsule or syrup (for midazolam only) with 240 milliliters of (tap) water. The volunteer will receive the study compound after an overnight fast (at least 8 hours no eating and drinking).

For Group 2, the actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen (Location UMCG) for 16 days (15 nights).

The volunteer will receive the study compound (VX-150 or placebo) under fasted condition, as a capsule with 240 milliliters of (tap) water. The volunteer will receive the study compound after an overnight fast (at least 8 hours no eating and drinking). Fasting will continue until 4 hours after administration of the study compound. Then the volunteer will receive a lunch.

Part C:

The actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen (Location UMCG) for 25 days (24 nights). However, based on the results of dosing on Day 1 and Day 6 it can be decided not to conduct dose administrations on Day 16 and Day 21. In that case, the volunteer will stay in the clinical research for 15 days (14 nights).

During the study the volunteer will receive VX-150 twice under fasted conditions, once under fed conditions and once with milk, as a capsule or tablet with 240 milliliters of (tap) water.

**Intervention**

Part A:

Sequence Treatment Day 1 Treatment Day 6 Treatment Day 11 Treatment Day 16
1 750 mg once (fasted) 1250 mg once (fasted) 1250 mg once (fed) 1250 mg once (milk)
2 1250 mg once (fasted) 750 mg once (fasted) 1250 mg once (milk) 1250 mg once (fed)

Part B:

Group Day(s) Treatment Dosage Form How often
1 -1 - midazolam 2 mg - syrup once
1-10 - VX-150 1250 mg*) or matching placebo (fed) - oral capsule once daily
11 - VX-150 1250 mg*) or matching placebo (fed), and - oral capsule once
- midazolam 2 mg (fed) - syrup

2 1-14 - VX-150 1750 mg*) or matching placebo (fasted) - oral capsule once daily

*) The dose level of VX-150 may be increased or decreased based on the data from Part A of the study. The volunteer will be informed by an amendment if the

dose will change.

Part C:

Sequence Treatment Day 1 Treatment Day 6 Treatment Day 16*) Treatment Day 21*)
1 1500 mg once 1500 mg once 1500 mg once 1500 mg once
(fasted) as a capsule (fasted) as a tablet (fed) as a tablet
(milk) as a tablet
2 1500 mg once 1500 mg once 1500 mg once 1500 mg once
(fasted) as a tablet (fasted) as a capsule (milk) as a tablet
(fed) as a tablet

*) The dosing on Day 16 and Day 21 will only proceed if data from Day 1 and Day 6 supports further evaluation of the tablet dosage form.

**Study burden and risks**

For Part A, B and C:

VX-150
As of November 15, 2016 approximately 141 healthy subjects, and 124 patients with osteoarthritis have received at least one dose of VX-150. Based on limited experience so far, there are no known side effects for the study compound. Overall, the study compound has been well tolerated in humans. There were some adverse events that occurred in subjects taking the study compound or an inactive placebo, but we do not know whether they were due to the study compound or other conditions. Some of these adverse events included:

• Headache
• Muscle or joint aches
• Rash
• Dizziness
• Fatigue
• Runny nose

Continued (blinded) analyses of 124 patients treated with osteoarthritis are ongoing. Safety observations included 5 serious adverse events in 3 subjects (pain in jaw with dyspnea, urinary tract infection, and urinary tract infection with sepsis (infection in the blood)), all of which were considered not related or unlikely related to study drug by the investigator. The most common adverse events that occurred in 4 or more subjects were headache (6 subjects), joint pain (6 subjects), dizziness (4 subjects), urinary tract infection (4 subjects), nasopharyngitis (4 subjects), and rash (4 subjects).

The study compound has been studied in laboratory animals (rats, dogs and monkeys). There have been no harmful side effects or toxicities at any tested

dose level. Decreased body weight and lower food consumption were observed in rats exposed to high doses of the study compound. These adverse effects and possibly others, still unknown, adverse effects may occur during the study.

And also for Part B:

Midazolam
Midazolam is already on the market. Midazolam is a short-acting sedative used prior to invasive diagnostic or surgical procedures. The most commonly reported side effects include the following:
• Nausea
• Vomiting
• Skin rash
• Agitation
• Prolonged sleepiness
• Abnormal heart beat
• Laryngospasm (sudden violent closure of the voice box)
• Rhonchi (rattling in the chest)
• Serious respiratory problems including respiratory depression, airway congestion or blockage and low oxygen level

• Less commonly reported adverse events include the following:
• Stopped breathing
• Decreased blood pressure
• Increased heart rate
• Hiccups
• Gagging
• Drooling
• Salivation
• Bad mood
• Excitation
• Aggression
• Mood swings
• Hallucinations (seeing or hearing things that are not there)
• Dizziness
• Confusion
• Lack of coordination
• Impaired speech
• Saying or doing things that you would not normally do
• Double vision
• Loss of balance
• Blurred vision

Midazolam has a boxed warning from the FDA because it can cause breathing difficulties. Midazolam has been associated with severe breathing difficulties, including slowed breathing, inability to breathe, airway obstruction and low oxygen most often when used together with other central

nervous system depressants (for example, pain medications). A significant decrease in the rate of your breathing can cause death if not treated correctly. If breathing is too slow after taking the study compound, the responsible physician will treat the volunteer, based upon PRA standard procedures. The single 2 mg oral dose of Midazolam is a standard dose used in drug-drug interaction studies and is less than the usual therapeutic dose of 10 to 20 mg. The dose is expected to be safe and well tolerated even when co-administered with VX-150.

# Contacts

**Public**
Vertex Pharmaceuticals Incorporated

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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 or femaile subjects
- 18-55 yrs, inclusive

- BMI: 18.0-31.0 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 or being a blood donor within 60 days from the start of the study. Blood donation (of approximately 1 pint [500 mL] or more) within 56 days before the first dose of study drug, or any significant loss of blood, as determined by the investigator, within 60 days before the first dose of study drug.

## Study design

### Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Crossover |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 27-01-2017 |
| Enrollment: | 40 |
| Type: | Actual |

### Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Midazolam |
| Generic name: | N/A |
| Registration: | Yes - NL outside intended use |

# Ethics review

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|---|---|
| Approved WMO Date: | 17-01-2017 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 25-01-2017 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 26-04-2017 |
| Application type: | Amendment |
| 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 | EUCTR2016-004495-21-NL |
| CCMO | NL60361.056.17 |