# A RANDOMIZED, DOUBLE-BLIND DRUG-DRUG INTERACTION STUDY TO ASSESS THE EFFECT OF ZOLPIDEM ON THE PHARMACOKINETICS, PHARMACODYNAMICS AND SAFETY AND TOLERABILITY OF DS-5565 IN HEALTHY SUBJECTS

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Primary:To examine the effect of zolpidem on the pharmacokinetics (PK) of DS-5565 in human plasmaTo assess the safety and tolerability of concomitant administration of DS-5565 and zolpidem as defined by the adverse event (AE) profile.Secondary:To...

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

## Summary

### ID

NL-OMON37431

**Source**
ToetsingOnline

**Brief title**
DS-5565 zolpidem interaction study

### Condition

- Other condition

**Synonym**
neuralgia, neuropathic pain

### Health condition

(zenuw) pijn bij diabetes en bij herpes (koortslip)

### Research involving
Human

## Sponsors and support

**Primary sponsor:** Daiichi Pharmaceutical
**Source(s) of monetary or material Support:** farmaceutische industrie

## Intervention

**Keyword:** Drug-Drug Interaction, DS-5565, Zolpidem

## Outcome measures

### Primary outcome

Pharmacodynamics: several cognitive tests

Pharmacokinetics: plasma DS-5565 and zolpidem concentrations, pharmacokinetic

parameters

Safety: adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination

### Secondary outcome

n/a

# Study description

### Background summary

DS-5565 is a new investigational compound that may eventually be used for the treatment of neuropathic pain associated with diabetes and herpes. DS-5565 is not registered as a drug but has been given to humans before. Zolpidem is a registered drug in the Netherlands and is used for the treatment of insomnia.

## Study objective

Primary:
To examine the effect of zolpidem on the pharmacokinetics (PK) of DS-5565 in human plasma
To assess the safety and tolerability of concomitant administration of DS-5565 and zolpidem as defined by the adverse event (AE) profile.

Secondary:
To examine the effect of DS-5565 on the PK of zolpidem in human plasma
To examine the effect of DS-5565 on the pharmacodynamics (PD) of zolpidem
To examine the effect of zolpidem on the PD of DS-5565
To assess the safety and tolerability of concomitant administration of DS-5565 and zolpidem with respect to clinical laboratory evaluation, vital signs, ECG, physical examination, respiratory function and the Columbia Suicide Severity Rating Scale (C SSRS).

## Study design

A randomized, double- blind, drug-drug interaction study in healthy volunteers

This study consists of 4 periods, during each period you will receive DS-5565 or placebo at a single dose of 10 mg and a single dose of 10 mg zolpidem or placebo.

Procedures and assessments during the study:
Screening and follow-up: clinical laboratory (including serum chemistry, hematology and urinalysis), vital signs, (including respiratory function), physical examination, 12-lead ECG, prior and concomitant medication, pregnancy test (females only), adverse effects (AE) reporting, C-SSRS;
at eligibility screening: FSH level, medical history, demography, weight, height, drug and alcohol screen, HBsAg, anti-HCV, anti-HIV 1/2 and pregnancy test (femalesonly);
to be repeated upon each admission: physical examination, weight, drug and alcohol screen, clinical laboratory, vital signs (incl. respiratory rate), 12-lead ECG, pregnancy test (females only), prior and concomitant medication and AE reporting

Blood sampling:
for pharmacokinetics of DS-5565 in plasma: pre-morning dose Day 1 until 24 hr post-dose Day 2
for pharmacokinetics of zolpidem in plasma: pre-morning dose Day 1 until 24 hr post-dose Day 2

Cognitive tests:
VSS-SF, Bond & Lader VAS, Body Sway, DSST, BARS: pre-morning dose Day 1 until

24 hr post-dose Day 2

Safety:
clinical laboratory, vital signs, respiratory measurements, ECG: pre-dose Day 1 until 24 hrs post-dose Day 2

**Intervention**

This study consists of 4 periods, during each period you will receive DS-5565 or placebo at a single dose of 10 mg for 3 occasions (as a morning and evening dose on Day 1 and as a morning dose on Day 2) and a single dose of 10 mg zolpidem or placebo in the morning of Day 2.

* Treatment A: DS-5565 placebo plus zolpidem placebo
* Treatment B: 10 mg DS-5565 plus zolpidem placebo
* Treatment C: DS-5565 placebo plus 10 mg zolpidem
* Treatment D: 10 mg DS-5565 plus 10 mg zolpidem

All participants will receive all 4 treatment combinations over the 4 periods, however the order in which this will occur will be determined by chance.

**Study burden and risks**

Four studies with 171 healthy volunteers had been performed to date, with single doses of DS-5565 from 3 to 75 mg and multiple doses from 5 to 25 mg. The most important adverse events reported were: dizziness, somnolence, nausea, headache, vision blurred, tremor, dysmenorrhoea, diarrhoea, palpitations, constipation, visual impairment, balance disorder, cognitive disorder, flatulence, gait disturbance, disturbance in attention, insomnia, and a change in liver function.
The most common side effects of zolpidem include drowsiness, dizziness, and a "drugged" feeling, which probably reflect the action of the drug. Other side effects include confusion, insomnia, euphoria, ataxia (balance problems), and visual changes. Zolpidem can cause abnormal behavior with confusion, paradoxical insomnia or "complex sleep-related behaviors," which may include sleep-driving (driving with no memory of having done so).
With the doses used in this study no serious adverse effects are expected. However, the occurrence of known or other effects cannot be excluded.

During the study several assessments will be conducted differing in extent and the nature of burden:
- Registration af adverse effects: During the entire investigation all adverse effects the subject experience and report will be documented.
- Blood draw, indwelling canula: During this study less then 500 ml of blood will be drawn. It is anticipated that on Day -1 an indwelling canula will be inserted for most of the blood sampling on Day 1 and 2. On the other days

during this study, blood will be drawn by direct puncture of the vein.
- Heart trace (ECG*s): ECG*s will be performed regularly at various time points: specifically on Days 1 and 2.
- Columbia Suicide Severity Rating Scale (C-SSRS): This is a questionnaire taken by the physician to asses any depressive or suicidal feelings the subjects may have at the screening visit. This test is a safety measure. However, there is currently no evidence that this investigational medicine will have this risk.
- Cognitive tests (Body Sway Test, several questionnaires, a neurological examination): These tests will be performed throughout the study but primarily on Day 2 of each period. On the day of arrival for period 1 the subject will receive training on these tests.
- Blood sample for DNA tests: On Day 1 a blood sample will be taken for possible DNA tests. Participation in this part of the study is optional. If the subjects do not wish to participate in this part of the study this will be stated so on the form at the end of the ICF.

## Contacts

**Public**
Daiichi Pharmaceutical

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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 (negative pregnancy test)
Age: 18-55 years (inclusive)
BMI: 19.0 - 30.0 (inclusive)

### Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/Aids. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters blood in the 10 months preceding the start of the study.

## Study design

### Design

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|---|---|
| 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): | 14-02-2012 |
| Enrollment: | 20 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | n/a |
| Generic name: | zolpidem |
| Registration: | Yes - NL intended use |

## Ethics review

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| Approved WMO Date: | 06-02-2012 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 10-02-2012 |
| 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 | EUCTR2011-006047-29-NL |
| CCMO | NL39503.056.12 |