# Single-dose, randomized, double-blind, two-way crossover study for the demonstration of pharmacodynamic equivalence of enoxaparin (100 mg/mL) 100-mg subcutaneous injection. Manufactured by Rovi (Spain) to Clexane (100 mg/mL) 100-mg subcutaneous injection manufactured by Sanofi (EU) in healthy volunteers.

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| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Coagulopathies and bleeding diatheses (excl thrombocytopenic) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON42485

**Source**
ToetsingOnline

**Brief title**
Rovi Enoxaparin Clexane bioequivalence study

## Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

**Synonym**
To treat or prevent a type of blood clot called deep vein thrombosis.

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** ROVI
**Source(s) of monetary or material Support:** Farmaceutische industrie

## Intervention

**Keyword:** healthy volunteers, pharmacodynamics, single-dose, subcutaneous injection

## Outcome measures

### Primary outcome

The primary objective is to demonstrate the pharmacodynamic (PD) equivalence

of enoxaparin (100 mg/mL) 100-mg SC injection manufactured by Rovi (Spain)

to Clexane (100 mg/mL) 100-mg SC injection manufactured by Sanofi (EU) in

healthy volunteers.

### Secondary outcome

The secondary objective is to evaluate the safety and tolerability of enoxaparin

(100 mg/mL) 100-mg SC injection manufactured by Rovi, Spain in healthy

volunteers.

# Study description

### Background summary

Enoxaparin works by preventing certain molecules in the blood, called clotting

factors, from working. Clotting factors are needed to form a clot (eg, on a cut or scratch). Enoxaparin can be used to treat existing blood clots, or stop clots from forming inside the body. Enoxaparin manufactured by the Sponsor is a new investigational compound which is being developed to treat or prevent a type of blood clot called deep vein thrombosis. Enoxaparin manufactured by the Sponsor has been administered to humans before.

Clexane® (manufactured by Sanofi) is no new drug; it is already available in the market. It is registered for the prevention and treatment of thrombosis. Clexane® is the brand name; the active substance is enoxaparin.

**Study objective**

The purpose of the study is to investigate the effect on the body of enoxaparin manufactured by the Sponsor (this is called pharmacodynamics) and to compare it with the pharmacodynamic effect of Clexane®. In addition, it will be investigated to what extent enoxaparin manufactured by the Sponsor is safe and tolerated. This study will be performed in a total of 46 healthy male and female volunteers.

The study will consist of 2 periods during which you will receive a single dose (100 milligrams [mg]) of enoxaparin manufactured by the Sponsor (= Treatment A) and a single dose (100 mg) of Clexane® (= Treatment B). Both study compounds will be given as a subcutaneous (under the skin) injection in the abdominal wall. The order in which you will receive the study compounds (first Treatment A followed by Treatment B, or the other way around) will be decided by chance (like flipping a coin).

**Study design**

The actual study will consist of 2 periods during which the volunteer will stay in the clinical research center in Groningen for
4 days (3 nights). The time interval between drug administration in the 2 periods will be at least 7 days. If you are a woman, your weight is < 45 kg, if you are a man, your weight is < 57 kg

**Intervention**

During the study you will receive a single dose of enoxaparin manufactured by the Sponsor and a single dose of Clexane®, both after an overnight fast (at least 10 hours no eating and drinking) as a subcutaneous injection.

On Day 1 of each period fasting will continue for at least 4 hours after administration of the study compound. Then you will receive a lunch. During fasting you are allowed to drink water with the exception of 1 hour prior to

until 1 hour after administration of the study compound.

**Study burden and risks**

The most common adverse events with enoxaparin manufactured by the Sponsor are: diarrhea, mild pain, swelling (ankles and feet), redness, irritation, bleeding or bruising at the injection site, nausea, anemia, upset stomach, increase in liver enzymes (AST and ALT levels) without clinical symptoms, thrombocytopenia (decrease of platelets with increased risk of bleeding) and allergic reactions such as rash, itching and swelling.

The most common adverse events with Clexane® are: bleeding, thrombocytosis (increased number of platelets in the blood) and an increase of liver enzymes in the blood. Serious cases of bleeding have been reported but this is not seen very often. The side effects described above were seen when Clexane® was given in patients with (high risk of developing) venous thromboembolic disorders, unstable angina, myocardial infarction or clot forming during hemodialysis who used the drug for multiple weeks. However, in this study only healthy volunteers will be included, who will receive a single dose.

# Contacts

**Public**
ROVI

Alfonso Gómez 45A
Madrid 28037
ES
**Scientific**
ROVI

Alfonso Gómez 45A
Madrid 28037
ES

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

- Healthy male or female.
- Between 18 and 45 years of age, inclusive.
- BMI is between 18 and 30 kilograms/meter2
- If you are a woman, your weight is > 45 kg, if you are a man, your weight is > 57 kg
- Nonsmoker

## Exclusion criteria

1. Subject has active or recurring clinically significant skin, head, ears, eyes, nose, throat, respiratory, cardiovascular, gastrointestinal, endocrine/metabolic, genitourinary, neurologic, hematologic, musculoskeletal, immunologic, allergic, psychological/psychiatric, or other disease requiring medical treatment
2. Subject is a woman who is pregnant or breastfeeding.
3. Subject has systolic blood pressure greater than 150 mm Hg or diastolic blood pressure greater than 90 mm Hg at Screening (confirmed upon repeat measurement).
4. Subject has a calculated (Cockroft & Gault formula) creatinine clearance less than 80 mL/minute and the value does not return to within reference range upon retest.
5. Subject has Hb <7.5 mmol/L and <8.5 mmol/L for female and male.
6. Subject has an active malignancy of any type other than nonmelanomatous skin malignancies.
7. Subject has any history of alcohol abuse or drug addiction.
8. Subject has any history of relevant drug and/or food allergies.
9. Subject has used any prescription drugs (with special attention to antiplatelet or anticoagulant medication, eg, acetyl salicylic acid, NSADs, clopidogrel, warfarin, acenocumarol, heparin, low molecular weight heparin, dabigatran, rivaroxaban, apixaban) or over-the-counter medication that may affect coagulation (including aspirin or NSAIDs) within 4 weeks before dosing, or any other over-the-counter medication (including vitamins, herbal supplements, or dietary supplements) within 2 weeks before dosing.
10. Subject has a positive test result for drugs of abuse (opiates, methadone, cocaine, amphetamines, cannabinoids, barbiturates, benzodiazepines, tricyclic antidepressants, oxycodone), cotinine, or alcohol.
11. Subject has a positive test result for human immunodeficiency virus (1 or 2) antibody, hepatitis B surface antigen, or hepatitis C virus antibody.
12. Subject has a positive test for fecal occult blood at Screening.
13. Subject has any history and/or current conditions of bleeding tendency such as: active

bleeding, known bleeding diathesis or hemostatic defects due to severe hepatic or renal disease; recent gastrointestinal or genitourinary bleeding (10 days before study entry); diabetic hemorrhagic retinopathy, or other hemorrhagic ophthalmic conditions.
14. Subject has a known history or family history of any relevant congenital or acquired coagulation disorder (eg, hemophilia, von Willebrand-Jürgens syndrome, or activated protein C resistance based upon Factor V Leiden mutation).
15. Subject has a history of thrombocytopenia, including heparin induced thrombocytopenia.
16. Subject has a known history of hypersensitivity to drugs with a similar chemical structure to enoxaparin sodium (eg, unfractionated heparin, LMWH), or to pork products.

# Study design

## Design

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

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 25-09-2015 |
| Enrollment: | 46 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Clexane |
| Generic name: | Clexane |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Enoxaparin |
| Generic name: | Enoxaparine |

# Ethics review

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| Approved WMO Date: | 15-09-2015 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 23-09-2015 |
| 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 | EUCTR2015-003489-10-NL |
| CCMO | NL54841.056.15 |