# Reversal of oral anticoagulants rivaroxaban and apixaban, by two different dosages of prothrombin complex concentrate (Cofact®).

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Reversibility of oral direct factor Xa inhibitors rivaroxaban and apixaban will be the same when a lower dosage of prothrombin complex concentrate (Cofact®) is used. Infusion with doses of 37.5 or 25 units/kg of PCC would be able to reverse the...

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|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestopt |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON21617

**Bron**
NTR

**Verkorte titel**
COFACTII

**Aandoening**

Healthy male subjects between 18 and 50 year who have no medical history of thrombotic disease or bleeding disorders will be included in the study. They must have a normal physical examination and laboratory screen tests. They will not use any medication at least 14 days before the study days.

### Ondersteuning

**Primaire sponsor:** S. Middeldorp
Academic Medical Center
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**Overige ondersteuning:** Sanquin

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

The primary outcome is the reversal (normalisation) of coagulation assays, at the end of oral f-Xa inhibitor administration and after the infusion of PCC or placebo.

# Toelichting onderzoek

### Achtergrond van het onderzoek

Rivaroxaban and apixaban lack a specific reversal agent. Fifty units/kg of 4-factor prothrombin complex concentrate (PCC, Cofact®) completely reversed the anticoagulant effect of rivaroxaban in healthy subjects. We hypothesized that infusion with doses of 37.5 or 25 units/kg of PCC would be able to reverse the anticoagulant effect of rivaroxaban and apixaban, both factor Xa inhibitors. In a randomized, double blind, placebo-controlled study, 12 healthy volunteers taking rivaroxaban 15 mg or apixaban 10 mg twice daily, received either a single bolus of PCC 37.5 units/kg, PCC 25 units/kg or placebo, with a wash-out period of 18 days in between infusions. The primary outcome was the effect of PCC on measures of thrombin generation, e.g. endogenous thrombin potential (ETP), after PCC or placebo infusion.

### Doel van het onderzoek

Reversibility of oral direct factor Xa inhibitors rivaroxaban and apixaban will be the same when a lower dosage of prothrombin complex concentrate (Cofact®) is used. Infusion with doses of 37.5 or 25 units/kg of PCC would be able to reverse the anticoagulant effect of rivaroxaban and apixaban.

### Onderzoeksopzet

Day -7: Randomization for PCC or saline,
baseline coagulation tests;

Days -7 to 0:

1. Group 1: Apixaban orally, 10 mg twice daily, for 7 and a half days (15 doses);

2. Group 2: Rivaroxaban orally, 15 mg twice daily, for 7 and a half days (15 doses).

Day 0: PCC/saline administration, scheduled coagulation tests;

Day 1: Scheduled coagulation tests.

**Onderzoeksproduct en/of interventie**

Intravenous administration of PCC (Cofact) 25 IU/kg or PCC (Cofact) 37.5 IU/kg or placebo (saline).

# Contactpersonen

## Publiek

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## Wetenschappelijk

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# Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Healthy male subjects as documented by laboratory screen tests (including HIV/HBV/HCV screening), personal medical history and normal physical examination;

2. Age ≥18 years, < 50 years;

3. No personal history of thrombotic disease/bleeding disorders;

4. No significant family history of thrombotic disease/bleeding disorders, such as recurrent thrombotic/bleeding events or thrombotic/bleeding events in the absence of any risk factors;

5. Able to provide written informed consent.

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. History of allergic reaction to blood products;

2. Current participation in any other investigational drug study or within the past 30 days;

3. Presence of any condition that, as judged by the investigator, would place the subject at increased risk of harm if he participated in the study.

## Onderzoeksopzet

### Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Enkelblind |
| Controle: | Placebo |

### Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestopt |
| (Verwachte) startdatum: | 15-10-2012 |
| Aantal proefpersonen: | 12 |
| Type: | Werkelijke startdatum |

## Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 02-08-2012 |
| Soort: | Eerste indiening |

# Registraties

## Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

## Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

## In overige registers

| Register | ID |
|---|---|
| NTR-new | NL3388 |
| NTR-old | NTR3559 |
| Ander register | : |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |

# Resultaten

**Samenvatting resultaten**
Reversal of Rivaroxaban and Dabigatran by Prothrombin Complex Concentrate: A Randomized, Placebo-Controlled, Crossover Study in Healthy Subjects.<br>
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