A study to evaluate the bioequivalence of Orfadin capsules 20 mg compared to Orfadin capsules 10 mg. An open-label, randomized, cross-over, single-dose study in healthy volunteers.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON39261

Source
ToetsingOnline

Brief title
Nitisinone 20 mg/10 mg capsule BE study

Condition

- Metabolic and nutritional disorders congenital

Synonym
hereditary tyrosinemia type 1

Research involving
Human

Sponsors and support

Primary sponsor: PRA International EDS
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: bioequivalence, hereditary tyrosinemia type 1

Outcome measures

Primary outcome

The area under the serum concentration vs. time profile during 72 hours after

dose (AUC72h).

The maximum serum concentration (Cmax).

Secondary outcome

AUC72h, AUC from time zero to infinity (AUC*), Cmax, time to reach Cmax (tmax),

terminal half-life (t*z), oral clearance (CL/F), and apparent volume of

distribution (Vz/F).

AEs, clinical chemistry, hematology, urinalysis.

Study description

Background summary

Orfadin® (nitisinone) is used in the treatment of hereditary tyrosinemia type 1 (HT-1), an inborn error of metabolism. (See Patient Information Leaflet (PIL), for more detailed information.) Before the market authorization of Orfadin (2002 in the US and 2005 in Europe) there was no available treatment for this fatal condition and patients therefore died very young. Since some patients have now reached adulthood, they need higher daily doses and use multiple capsules of 10 mg nitisinone. The new 20-mg strength tested in this study is easier to use.

Study objective

The primary purpose of the study is to investigate whether the new 20 mg capsule of Orfadin® (nitisinone) has a similar bioavailability in the body (gives the same concentration in the blood) as two of the marketed capsules of 10 mg.
The secundary purpose is to investigate the safety of the nitisinone capsules.

Study design

This is an open-label, randomized 2-way crossover study with 21-day washout between doses.

Intervention

All volunteers will receive, in randomized order:
- 20 mg nitisinone as 1 capsule of 20 mg
- 20 mg nitisinone as 2 capsules of 10 mg

Study burden and risks

During the study a number of assessments will be performed that may be considered more or less stressfull.
These are:
- Bloodsampling via venopunction and intravenous cannule
- ECG
- slit-lamp examination

Contacts

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Eligibility criteria

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

Inclusion criteria

healthy male and female subjects
18-55 yrs, inclusive
BMI: 18.5-30.0 kg/m2, inclusive
smoking <<= 10 cigarettes per day

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 > 50 mL within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-04-2013
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Orfadin
Generic name:	Nitisinone
Product type:	Medicine
Brand name:	Orfadin
Generic name:	Nitisinone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-04-2013
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	2012-005552-42
CCMO	NL44365.056.13