A randomized, four-way crossover, comparative bio-availability study of branded (Neurontin®) and three generic 800 mg gabapentin labels in healthy subjects under fasting conditions.

Published: 19-07-2011
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The aim of this study is to investigate the possible consequences of generic-generic substitution of gabapentin, a frequently used anti-epileptic drug.

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

Summary

ID

NL-OMON35125

Source
ToetsingOnline

Brief title
Comparative bio-availability study with gabapentin.

Condition

- Other condition
- Peripheral neuropathies

Synonym
epilepsy, neuropatic pain

Health condition

epilepsie

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: branded, gabapentin, generic, pharmacokinetics

Outcome measures

Primary outcome

To compare the pharmacokinetic profile of gabapentin from the Neurontin® 800 mg tablet and three generic gabapentin 800 mg tablets after single dose administration of 800 mg in healthy volunteers under fasting conditions.

The main endpoints will be the 90% confidence intervals of the ratio of least-squares means of the pharmacokinetic parameters AUC0-t, AUCinf, and Cmax of two tested gabapentin products (for all combinations among the four products).

Secondary outcome

To compare the tolerability and safety of gabapentin from the Neurontin® 800 mg tablet and three generic gabapentin 800 mg tablets after single dose administration of 800 mg in healthy volunteers under fasting conditions.

Study description

Background summary

In clinical practice, generic drugs (generics) are often interchanged, whereas factual data regarding generic-generic interchangeability are lacking. Under

these conditions, the so-called *shift* or *drift* problem that may occur when generics are interchanged may be reason for concern; while generics are exchangeable with the innovator product, generics themselves may not be, which may lead to loss of efficacy or increased toxicity. This problem may be relevant for certain drugs with a narrow therapeutic window, including anti-epileptic drugs, where seizure control may be lost or side-effects may increase when patients switch from one generic to another.

Study objective

The aim of this study is to investigate the possible consequences of generic-generic substitution of gabapentin, a frequently used anti-epileptic drug.

Study design

Randomized, four-period, four-treatment, crossover, balanced, single dose comparative oral bioavailability study in healthy, adult, subjects under fasting conditions.

Intervention

There will be 4 periods of administration of gabapentin, each separated by one week. Each volunteer will receive a single dose of 800 mg of gabapentin after an overnight fast (either Neurontin® or one of the 3 generic gabapentin tablets in a randomized order) at the beginning of each period, i.e., on Day 1, Day 8, Day 15, or Day 22.

Study burden and risks

Study participants will undergo a medical history taking, physical examination (2 times), routine laboratory blood (6 times) and urine tests (2 times), urine pregnancy tests (5 times, females only), urine testing for recreational drugs (5 times), alcohol breath tests (5 times), a 12-lead ECG (2 times) and measurements of vital signs, i.e. heart rate, blood pressure, temperature and respiratory rate (38 times) and venous blood sampling for analysis of gabapentin plasma concentration (12 times by venapunction, 56 times by peripheral venous catheter). A total of 306 mL of blood will be sampled from each participant during the study. A repeated blood or urine sampling may be performed when deemed necessary to check or follow up an abnormal result from a previous sample.
After a screening visit, each participant will visit the trial centre 4 times for a night (from 22 pm) and day (till 12 hours after dosing), and will fast for at least 10 hours before dosing until 4 hours post-dose. Water will be restricted for one hour before and after dosing.
Gabapentin has been demonstrated to be safe in humans within the effective

dosing range from 900 to 3600 mg/day. Participants will not benefit directly from participation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

*male or female volunteer, 18-55 years of age;
*non-smoking (for at least 3 months) or moderately smoking, i.e. less than 10 cigarettes a day;
*weighing in the normal range according to accepted normal values of BMI Chart (18-30kg/m2);
*in a healthy condition, as assessed bij the investigator based on medical history, physical exam, vital signs, routine laboratiry tests and 12-lead ECG;
*females of childbearing potential should either be sexual inactive for 14 days prior to the

first dose and throughout the study or be using an acceptable birth control method;
*voluntary consenting to participate in the study.

Exclusion criteria

*history or presence of significant cardiovascular, pulmonary, hepatic, renal, hematologic, gastrointestinal, endocrine, immunologic, dermatologic, neurologic, or psychiatric disease;
*a positive test result for HIV, hepatitis B and C;
*history or presence of alcoholism or drug abuse within the past year or hypersensitivity or idiosyncratic reaction to gabapentin or any other anticonvulsive agents;
*female subjects who are pregnant or lactating;
*subjects who have a variable, instable nutrition pattern;
*subjects who have donated blood within the last 2 months, or who have donated plasma within the last 14 days;
*subjects who have participated in another clinical trial within 28 days prior to start to the first dose.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-09-2011
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Gabapentin Apotex
Generic name:	gabapentin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Gabapentin Centrafarm
Generic name:	gabapentin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Gabapentin PCH
Generic name:	gabapentin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Neurontin
Generic name:	gabapentin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-07-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-09-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-09-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-10-2011

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	EUCTR2011-002335-26-NL
CCMO	NL37405.056.11