Gabapentin 800 mg tablets, four-way crossover, fasting bioavailability study in healthy subjects.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25575

Source
Nationaal Trial Register

Brief title
Bioavailability of gabapentine

Health condition

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.

Sponsors and support

Primary sponsor: Maastricht University Medical Center +
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Tel: 043 388 1766
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Source(s) of monetary or material Support: College ter Beoordeling van Geneesmiddelen-Medicine Evaluation Board
579 Radboud University Nijmegen Medical Center
Antony van Leeuwenhoeklaan 5
Nijmegen
The Netherlands

Intervention

Outcome measures

Primary outcome

To compare the pharmacokinetic profile of gabapentin of 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 of 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

Rationale:

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.

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

Objectives:

To assess the pharmacokinetic profile, tolerability and safety of gabapentin of the brand 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 design:

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

Study population:

The study population will be non-smoking or moderate smoking healthy human volunteers with an age range from 18 - 55 years old.

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 a brand Neurontin® tablet or one of the 3 generic gabapentin tablets in a randomized order) at the beginning of each period.

Main study endpoints:

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).

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

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.

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

All subjects will be checked-in at the unit of DRUM at 10 pm for an overnight stay without intake of any food and drink at least after 10 pm. Drug screen test, pregnancy test and alcohol breath test are repeated between check-in and dosing. Limited lab safety (creatinin, total bilirubin, alkaline phosphatase, AST, ALT, gamma GT and glucose) is repeated within 2 hours before dosing. They will be housed in the unit to at least 12 hours post dose in each period. During this period, subjects will not be allowed to leave the unit. Subjects will return to the unit for the 24-, 36- and 48-hour blood sample.

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 a brand Neurontin® tablet or one of the 3 generic gabapentin tablets in a randomized order) at the beginning of each period.

Contacts

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Eligibility criteria

Inclusion criteria

Subject candidates must fulfill all of the following inclusion criteria to be eligible for participation in the study, unless otherwise specified:

1. Male or female volunteers, 18-55 years of age;

2. Non-smoking (for at least 3 months) or moderately smoking, i.e. less than 10 cigarettes a day (for at least 3 months);

3. Weighing within the normal range according to accepted normal values of the Body Mass Index Chart (18-30 kg/m2);

4. In a healthy condition, as assessed by the investigator based on medical history, physical exam, vital signs, routine laboratory tests and 12-lead ECG;

5. Females of childbearing potential should either be sexually inactive (abstinent) for 14 days prior to the first dose and throughout the study or be using an acceptable birth control methods;

6. Voluntarily consenting to participate in the study.

Exclusion criteria

Subject candidates must not be enrolled in the study if they meet any of the following criteria:

1. History or presence of significant cardiovascular, pulmonary, hepatic, renal, hematologic, gastrointestinal, endocrine, immunologic, dermatologic, neurologic, or psychiatric disease;

2. A positive test result for HIV, hepatitis B and C;

3. In addition, history or presence of: Alcoholism or drug abuse within the past year; Hypersensitivity or idiosyncratic reaction to gabapentin or any other anti-convulsive agents;

4. Female subjects who are pregnant or lactating;

5. Subjects who have a variable, instable nutrition pattern;

6. Subjects who have donated blood within the last 2 months, or who have donated plasma within the last 14 days;

7. Subjects who have participated in another clinical trial within 28 days prior to the first dose.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2011
Enrollment:	24
Type:	Actual

Ethics review

Positive opinion

Date:	26-06-2011
Application type:	First submission

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
NTR-new	NL2823
NTR-old	NTR2964
Other	Drug Research Unit Maastricht : DRUM11-GABA
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A