A SINGLE-CENTER, OPEN-LABEL, ONE-SEQUENCE, THREE-PERIOD CROSSOVER STUDY TO EVALUATE THE PHARMACOKINETICS OF HP-3040 PATCHES (TOLTERODINE TRANSDERMAL DRUG DELIVERY SYSTEM) FOLLOWING 168-HR APPLICATION COMPARED TO SINGLE-DOSE DETROL® LA 2 MG (TOLTERODINE TARTRATE EXTENDED RELEASE CAPSULE) IN HEALTHY ADULT MALE SUBJECTS

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

Summary

ID

NL-OMON37479

Source
ToetsingOnline

Brief title
HP-3040 transdermal patch study

Condition

- Other condition

Synonym
involuntary leakage of urine, loss of bladder control

Health condition

urine incontinentie

Research involving
Human

Sponsors and support

Primary sponsor: Noven Pharmaceuticals, Inc
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: HP-3040, tolterodine, transdermal patch, urinary incontinence

Outcome measures

Primary outcome

Pharmacokinetics: tolterodine, 5-hydroxymethyl tolterodine and the combined

active moiety (tolterodine + 5 hydroxymethyl tolterodine) serum concentrations

and PK parameters

Dermal evaluations: presence and severity of skin irritation and discomfort,

patch adhesion, amount of adhesive residue at application site

Other evaluations: difficulty of patch removal from the liner, residual drug

analysis

Safety: AEs, vital signs, ECG, clinical laboratory assessments, physical

examination

Secondary outcome

n/a

Study description

Background summary

The drug to be given is an existing compound, tolterodine, in a new application form (transdermal patches). Tolterodine is used to treat urinary incontinence. In this study a new administration method of tolterodine, the HP-3040 transdermal patch, will be tested. This is the first time tolterodine will be administrated to humans in this form of transdermal patches. In addition to tolrerodine in the new application form (transdermal patches), you will receive single dose of registered Detrol® LA (containing tolterodine tartrate) in the form of a capsule.

Study objective

The purpose of the study is to investigate how quickly and to what extent tolterodine is absorbed and eliminated from the body (this is called pharmacokinetics) when it is administrated by using a HP-3040 transdermal patch. Moreover, the relative bioavailability (measurements of the amount of drug that is actually absorbed) of tolterodine will be investigated when it is administrated by using a HP-3040 transdermal patch. Furthermore, the pharmacokinetic profile of HP-3040 transdermal patches will be compared to oral administration of Detrol® LA. In addition, the safety and tolerability of the HP-3040 transdermal patch will be investigated.

Study design

This is a single-center, open-label, 1-sequence, 3-period, comparative crossover study in 12 healthy adult male subjects.

Procedures and assessments:
Screening and follow-up: physical examination, weight, vital signs (blood pressure, pulse rate and body temperature), 12-lead electrocardiogram (ECG), clinical laboratory (clinical chemistry, hematology and urinalysis) and previous and concomitant medication

Only at screening: medical history, demographics, height, measurement of intraocular pressure, drug and alcohol screen and serology (HBsAg, HCV and HIV)

Repeated at admission in each period: clinical laboratory (clinical chemistry, hematology and urinalysis), drug and alcohol screen, adverse events and previous and concomitant medication

Bloodsamping:
For PK tolterodine, 5-hydroxymethyl tolterodine and the combined active moiety in serum:
Treatment A: before dosing untill 48 hours after dosing
Treatment B and C: before dosing untill 240 uur after dosing
For genotyping of CYP2D6: on Day 1 of period 1 (before dosing)

Residual drug:
Used patches will be collected in the labeled vials following the procedures provided by the Sponsor and shipped
back to the Sponsor for analysis of residual ditolterodine (Treatments B and C)

Dermal assessments:
skin irritation: immediately before application untill 240 hours after application (Treatments B, C)
discomfort: untill 168 hours after application (Treatments B, C)
patch adhesion: untill 168 hours after application (Treatments B, C)
adhesive residue at application site: immediately after patch removal (Treatments B, C)

Safety assessments:
AEs: throughout the study
clinical laboratory assessments (including clinical chemistry, hematology and urinalysis): prior to discharge on Day 3 (period 1) and 11 (period 2 and 3)
vital signs (including blood pressure, pulse rate and body temperature) and ECG: pre-dose untill 48 hours postdose/
240 hours after patch application

Intervention

Treatment A: one Detrol® LA, 2 mg oral capsule (2 mg tolterodine tartrate) administered under fasting conditions
Treatment B: one HP-3040-75 transdermal patch (containing 75 mg tolterodine tartrate) applied for 168 hours on the lower abdomen, under fasting conditions.
Treatment C: two HP-3040-75 transdermal patches (containing 150 mg tolterodine tartrate) applied for 168 hours on the lower abdomen, under fasting conditions.

Study burden and risks

As the HP-3040 transdermal patch will be administered to man for the first time in this study, adverse effects in man have not been reported up to now. As with other transdermal system products, the use of the patches may occasionally lead

to symptoms of contact dermatitis such as redness, rash, eruption, flare, itching, pigmentation, skin irritation and loss of hair at the site of application.

Detrol® LA is a registered drug, containing tolterodine as active ingredient. The most (frequently) reported adverse effects after administration with capsules include dry mouth, skin and eyes, difficulty seeing, stomach and intestinal problems, difficult urination, fatigue, headache, dizziness and accumulation of fluid in for example the ankles, legs and arms.
Adverse effects that may occur, to a more or lesser extent, wearing one or two transdermal patches (treatment C): abnormal heartbeat, sensitivity to light, constipation, full bladder, decreased frequency of urination, imbalance, reduced state of consciousness and hallucinations.

Registration af adverse effects: During the entire investigation all adverse effect you report will be documented.

Blood draw, indwelling canula: During this study approximately 569 ml of blood will be drawn. In period 1, blood will be drawn until 48 hours after administration of Detrol® LA (thus until Day 3). In period 2 and 3 blood will be drawn until 240 hours (thus until Day 11) after patch application.
It is anticipated that on Day -1 of each period an indwelling canula will be inserted for most of the blood sampling on Day 1 and 2. On the other days during this study, blood will be drawn by direct puncture of the vein.

Measurement of intraocular pressure (IOP): During the screening the intraocular pressure will be measured. A trained physician will perform the measurement. Using specific equipment, a small puff of air will be blown on to your eye. This is not painful. You are sure to blink with your eyes and may experience a small fright reflex. In the event that a measurement is not good due to movement or blinking of the eye, it will be repeated.

Heart trace (ECG*s): ECG*s will be made regularly.

Blood sample for DNA tests: On Day 1 a blood sample will be taken for possible DNA tests. Participation in this part of the study is optional. If you do not wish to participate in this part of the study please state so on the form at the end of this document. Refusal to participate will involve no penalty or loss of benefits to which you would otherwise be entitled.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male subjects
18-45 yrs, inclusive
BMI: 18.0-30.0 kg/m2, inclusive
non-smoking or a light smoker (less than 5 cigarettes per day for minimal 6 months)
light skin color

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 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
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-02-2012
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Detrol LA
Generic name:	tolterodine tartrate

Ethics review

Approved WMO

Date:	10-02-2012
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	EUCTR2012-000376-42-NL
CCMO	NL39629.056.12