AN OPEN-LABEL, STUDY WITH THREE PROPORTIONATE SIZES OF HPS-328 PATCH APPLIED FOR 168 HOURS AND ONE ORAL DOSE REGIMEN OF 5 MG BISOPROLOL FUMARATE ONCE DAILY FOR ONE WEEK, TO INVESTIGATE THE PHARMACOKINETICS, TOLERABILITY AND SAFETY OF HPS-328 PATCHES IN HEALTHY MALE SUBJECTS

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

Summary

ID

NL-OMON36691

Source
ToetsingOnline

Brief title
HPS-328 transdermal patch study

Condition

- Other condition

Synonym
hypertensia

Health condition

hoge bloeddruk

Research involving
Human

Sponsors and support

Primary sponsor: Hisamitsu Pharmaceutical
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: bisoprolol, HPS-328, hypertension, transdermal patch

Outcome measures

Primary outcome

- Pharmacokinetics

- Safety

- ambulatory blood Pressure Recordings and pulse

Secondary outcome

n.a.

Study description

Background summary

The drug to be given is an existing compound, bisoprolol (registered under the tradename Emcor®) in a new application form (transdermal patches).
Bisoprolol belongs to the class of *-blockers and can reduce blood pressure and

heart rate, and decrease the oxygen-consumption of the heart muscle. Therefore it can be used, and is in fact widely used, for the treatment of high blood pressure and pain on the chest as a result of a lack of oxygen of the heart muscle (angina pectoris).
In this study a new administration method of bisoprolol, in the form of transdermal application, is tested.
An advantage of this new administration system would be the ease of use for the patient, with a once weekly application of a dermal patch in stead of daily oral tablet ingestion. Another possible advantage could be the much more stable blood concentration of the transdermal administration, compared with the rather strong variation of the usual once daily oral dose regimen.

Study objective

The purpose of the study is to investigate how safe the compound is and how well the compound is tolerated when it is applied in the form of transdermal patches. The study will also investigate how quickly and to what extent bisoprolol is absorbed and eliminated from the body, when it is administered in the form of transdermal patches (during 168 hours), for Group 1 in comparison to bisoprolol fumarate in the form of tablets.

Study design

Group 1: in one period the study drug will be administered as tablet (sinlge daily dose of 5 mg for the duratian of 7 days); in the other periode the study drug will be administered as transdermal patch (singe dose of 90 mg). The transdermal patch will be removed after 168 hours.
Group 2: the volunteers of this group will receive two transdermal patches for 168 hours with a total dose of 180 mg study drug.
Group 3: the volunteers of this group will receive four transdermal patches for 168 hours with a total dose of 360 mg study drug.

Procedures and assessments:
Screening and follow-up:
clinical laboratory, vital signs, physical examination, body weight, body height (screening only), 12-lead ECG; at eligibility screening: medical history, alcohol and drug screen and nicotine metabolites, HBsAg, anti HCV, anti-HIV 1/2; alcohol and drug screen and nicotine metabolites, clinical laboratory, vital signs and 12-lead ECG to be repeated upon admission.

Group 1:
Observation period:
2 periods, in the clinkic from 40 uur before first administration of study drug until 240 hours after administration of the study drug on Day 1.

Blood sampling:

patch administration period for pharmacokinetics of bisoprolol: pre-dose (before application) and 2, 4, 6, 8, 12, 18, 24, 28, 32, 40, 48, 60, 72, 74, 76, 78, 80, 84, 90, 96, 120, 144, 146, 148, 150, 152, 156, 162, 168 (before removal), 170, 172, 176, 180, 192, 204, 216 and 240 h post patch application
oral administration period for pharmacokinetics of bisoprolol: pre-dose (before 1st dosing) and 0.5, 1, 2, 3, 4, 6, 8, 10, 12, 24 (before 2nd dosing), 27, 48 (before 3rd dosing), 51, 72 (before 4th dosing), 72.5, 73, 74, 75, 76, 78, 80, 82, 84, 96 (before 5th dosing), 99, 120 (before 6th dosing), 123, 144 (before 7th dosing), 144.5, 145, 146, 147, 148, 150, 152, 154, 156, 168, 180, 192, 204, 216 and 240 h after 1st dosing

Urine sampling:
for pharmacokinetics of bisoprolol: pre-dose and intervals 0-24, 24-48, 48-72, 72-96, 96-120, 120-144, 144-168, 168-192, 192-216 and 216-240 hours post dosing for both periods.

Ambulatory Blood Pressure Recordings: for 24 hours on Days -1, 1, 4 and 7 (first 16 hours every half hour, last 8 hours once per hour) in both study periods.

Safety assessments:
adverse events: throughout the study;
vital signs: at screening, and at admission, once daily on Days 1 to 11 in both study periods; clinical
ECG: at screening and admission, at pre-dose and 1, 2, 3, 5, 7 and 12 h post-dose and on Days 1, 4 and 7 and once on Days 2, 3, 5, 6, 8, 9, 10 and 11; on day -1 on the scheduled timepoints of day 1 for both study periods.
clinical laboratory: at screening and at admission and on Day 11 in both study periods
visual inspection application site: screening, 0 h (before application), at 169, 192, 204, 216 and 240 h after application;
adhesion evaluation: 2, 8, 24, 48, 72, 96, 120, 144, and 168 hours after application

Bioanalysis: analysis of plasma and urine bisoprolol samples using validated methods by Sponsor

Group 2 and 3:
In the clinic from 40 hours before first administration until 240 hours after administration of the study drug on Day 1.

Blood sampling:
for pharmacokinetics of bisoprolol: pre-dose (before application) and 2, 4, 6, 8, 12, 18, 24, 28, 32, 40, 48, 60, 72, 74, 76, 78, 80, 84, 90, 96, 120, 144, 146, 148, 150, 152, 156, 162, 168 (before removal), 170, 172, 176, 180, 192, 204, 216 and 240 h post patch application

Urine sampling:
for pharmacokinetics of bisoprolol: pre-dose and intervals 0-24, 24-48, 48-72, 72-96, 96-120, 120-144, 144-168, 168-192, 192-216 and 216-240 hours post dosing

Ambulatory Blood Pressure Recordings: for 24 hours on Days -1, 1, 4 and 7 (first 16 hours every half hour, last 8 hours once per hour).

Safety assessments:
adverse events: throughout the study;
vital signs: at screening, and at admission, once daily on Days 1 to 11
ECG: at screening and admission, at pre-dose and 1, 2, 3, 5, 7 and 12 h post-dose and on Days 1, 4 and 7 and once on Days 2, 3, 5, 6, 8, 9, 10 and 11; on Day -1 on the scheduled timepoints of Day 1.
clinical laboratory: at screening and at admission and on Day 11 in both study periods
visual inspection application site: screening, 0 h (before application), at 169, 192, 204, 216 and 240 h after application;
adhesion evaluation: 2, 8, 24, 48, 72, 96, 120, 144, and 168 hours after application

Bioanalysis: analysis of plasma and urine bisoprolol samples using validated methods by Sponsor

Intervention

Active compound: bisoprolol in transdermal patch (HPS-328, 90 mg bisoprolol per 15 cm2) or bisopolol fumarate as tablets, 5 mg per tablet (Emcor®).

Study burden and risks

Procedures: pain, light bleeding, heamatoma, possibly an infection, irritation patch.

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

- age 40 - 65 year
- BMI 18.0 - 29.9
- caucasian

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 60 days from the start of the study or in case of donating more than 1 liter 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):	26-01-2011
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Emcor
Generic name:	Bisoprolol
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	11-01-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-01-2011
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	EUCTR2010-023848-33-NL
CCMO	NL35280.056.11