ISRCTN96078237 https://doi.org/10.1186/ISRCTN96078237

Bioavailability and tolerability study of two new DHEP-medicated plasters in comparison with the marketed DHEP medicated plaster 1.3% (Flector®)

Submission date
11/01/2017

Recruitment status
No longer recruiting

Registration date
19/01/2017

Overall study status
Completed

Last Edited
19/01/2017

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The Ibsa DHEP medicated plaster contains diclofenac, an anti-inflammatory pain killer. The aim of this study is to assess the amount of diclofenac in the bloodstream after the application for two consecutive days of two new DHEP medicated plasters that contain higher amounts of diclofenac (2.6% and 3.9% DHEP), in comparison with the marketed DHEP medicated plaster 1.3%. The higher amount of diclofenac should improve the painkiller/anti-inflammatory effects of the plaster by increasing the amount of diclofenac at the application site, while keeping the amount in the rest of the body very low so as to avoid side effects.

Who can participate?
Healthy volunteers aged 18-55

What does the study involve?
Participants attend three study periods where they stay at the clinical centre from the late afternoon before the plaster application (study day -1) until the morning of day 3. The three study periods are separated by breaks of at least 7 days. In each study period one DHEP medicated plaster (either 1.3%, 2.6% or 3.9%) is applied to the participant's arm once a day for two consecutive days. The amount of diclofenac in the bloodstream is measured for 24 hours after plaster application, and any side effects are recorded.

What are the possible benefits and risks of participating?
No potential benefits expected for participating in this study. There are no significant risks related to the DHEP-medicated plasters. The side effects most frequently reported are mild to moderate skin reactions at the site of plaster application.

Where is the study run from?
CROSS Research Phase I Unit (Switzerland)

When is the study starting and how long is it expected to run for?
May 2015 to March 2016

Who is funding the study?
IBSA Institut Biochimique S.A (Switzerland)

Who is the main contact?
Dr Milko Radicioni

Contact information

Type(s)
Scientific

Contact name
Dr Milko Radicioni

ORCID ID
http://orcid.org/0000-0002-3940-8375

Contact details
CROSS Research Phase I Unit
Via F.A. Giorgioli 14
Arzo
Switzerland
CH-6864

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Study CRO-PK-15-305 - Sponsor code 15CH-Fpf03

Study information

Scientific Title
Bioavailability and tolerability study of two new DHEP-medicated plasters in comparison with the marketed DHEP-medicated plaster 1.3% (Flector®): a single-centre, multiple-dose, randomised, three-way cross-over, open-label, bioavailability and tolerability study

Study objectives
Compare the pharmacokinetic (PK) profile and tolerability of diclofenac in plasma after o.d. application for 2 consecutive days of DHEP-medicated plaster (test 1, 2.6% or test 2, 3.9% or reference, 1.3%) in healthy male and female volunteers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Cantonal Ethics Committee, Ticino, Switzerland, 08/02/2016, ref: CE3010
2. Federal Health Authorities (Swissmedic), 29/01/2016, ref: 2016dr1021

Study design
Single-centre multiple-dose randomised three-way cross-over open-label bioavailability and tolerability study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
No participant information sheet available’

Health condition(s) or problem(s) studied
DHEP-medicated plaster

Interventions
Test treatment 1: Diclofenac-N-(2-hydroxyethyl)-pyrrolidine (DHEP) medicated plaster 2.6%, corresponding approximately to 280 mg of diclofenac sodium
Test treatment 2: Diclofenac-N-(2-hydroxyethyl)-pyrrolidine (DHEP) medicated plaster 3.9%, corresponding approximately to 420 mg of diclofenac sodium
Reference formulation: Diclofenac-N-(2-hydroxyethyl)-pyrrolidine (DHEP) medicated plaster DHEP 1.3%, corresponding approximately to 140 mg of diclofenac sodium

The study consisted of a screening visit, a treatment phase of three study periods separated by a wash-out interval of at least 7 days between the second plaster application of the previous period and the first application of the next period and a final visit/early termination visit (ETV). One DHEP medicated plaster (test 1, 2.6% or test 2, 3.9% or reference, 1.3%) was applied once a day for 2 consecutive days in the three study periods according to a three-way cross-over randomised study design. The plasters were applied to the same application area of the same arm in the three study periods.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Diclofenac-N-(2-hydroxyethyl)-pyrrolidine (DHEP)

Primary outcome measure
Pharmacokinetic profile of diclofenac in plasma after o.d. application for 2 consecutive days of DHEP-medicated plaster - plasma concentrations of diclofenac measured on day 1 at pre-dose (0) and on days 2-3 at pre-dose (0) and 1, 2, 3, 4, 6, 8, 10, 12, 16, 20 and 24 h post-dose (13 samples each study period)

Secondary outcome measures
Safety and tolerability after o.d. application for 2 consecutive days of DHEP-medicated plaster, based on the following assessments:
1. Record of adverse events, assessed throughout the study
2. Vital signs: blood pressure (BP) and heart rate (HR), measured at rest (5 min in sitting position) by the investigator or his deputy at the screening visit, on day -1, as well as on day 3 at 24 h post-dose in each period, and in case of ETV. The vital signs measurement at 24 h post-dose of day 3, period 3, was considered as the final assessment
3. Electrocardiograms: a 12-lead resting ECG performed in supine position and interpreted by the investigator at screening
4. Physical examination and body weight: a physical examination, including measurement of BW, performed at screening and final visit/ETV
5. Routine haematology, blood chemistry and urinalysis laboratory tests performed, under fasting conditions, at screening and at the final visit/ETV
6. Local tolerability, assessed giving a score according to the a 4-grade scale to each of the following parameters: Application site erythema, Application site dryness, Application site swelling, Application site exfoliation (If the score assigned was 1, 2 or 3, the local reaction was treated as an AE with intensity mild (score 1), moderate (score 2) or severe (score 3), while the severity of 0 score was none
7. Plaster adhesiveness, assessed using the 5-point scale in compliance with FDA suggested scoring system for adhesion of transdermal patches, immediately before plaster removal on days 2 and 3

Overall study start date
15/05/2015

Completion date
23/03/2016

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the study
2. Males/females, 18-55 years old inclusive
3. Body Mass Index (BMI): 18.5-30 kg/m2 inclusive
4. Vital signs: systolic blood pressure (SBP) 100-139 mmHg, diastolic blood pressure (DBP) 50-89 mmHg, heart rate (HR) 50-90 bpm, measured after 5 min at rest in the sitting position
5. Full comprehension: ability to comprehend the full nature and purpose of the study, including possible risks and side effects; ability to co-operate with the investigator and to comply with the requirements of the entire study
6. Contraception and fertility (females only): females of child-bearing potential were required to use at least one of the following reliable methods of contraception:

6.1. Hormonal oral, implantable, transdermal, or injectable contraceptives for at least 2 months before the screening visit
6.2. A non-hormonal intrauterine device [IUD] or female condom with spermicide or contraceptive sponge with spermicide or diaphragm with spermicide or cervical cap with spermicide for at least 2 months before the screening visit
6.3. A male sexual partner who agreed to use a male condom with spermicide
6.4. A sterile sexual partner
Female participants of non-child-bearing potential or in post-menopausal status for at least 1 year were admitted. For all female subjects, pregnancy test result had to be negative at screening and at each scheduled evaluation

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
Twelve (12) healthy male and female subjects

Key exclusion criteria
1. Electrocardiogram (12-leads, supine position): clinically significant abnormalities
2. Physical findings: clinically significant abnormal physical findings which could interfere with the objectives of the study
3. Laboratory analyses: clinically significant abnormal laboratory values indicative of physical illness
4. Allergy: ascertained or presumptive hypersensitivity to the active principle and/or formulations' ingredients; history of anaphylaxis to drugs or allergic reactions in general, which the investigator considered could affect the outcome of the study
5. Diseases: significant history of renal, hepatic, gastrointestinal, cardiovascular, respiratory, skin, haematological, endocrine or neurological diseases that could interfere with the aim of the study
6. Medications: medications, including over the counter medications and herbal remedies for 2 weeks before the start of the study. Hormonal contraceptives for females were allowed
7. Investigative drug studies: participation in the evaluation of any investigational product for 3 months before this study. The 3-month interval was calculated as the time between the first calendar day of the month that followed the last visit of the previous study and the first day of the present study
8. Blood donation: blood donations for 3 months before this study
9. Drug, alcohol, caffeine, tobacco: history of drug, alcohol [>1 drink/day for females and >2 drinks/day for males, defined according to the USDA Dietary Guidelines 2010)], caffeine (>5 cups coffee/tea/day) or tobacco abuse (>10 cigarettes/day)

10. Drug test: positive result at the drug test at screening
11. Alcohol test: positive alcohol breath test at day -1
12. Diet: abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits in the 4 weeks before this study; vegetarians
13. Pregnancy (females only): positive or missing pregnancy test at screening or day -1, pregnant or lactating women

Date of first enrolment
29/02/2016

Date of final enrolment
01/03/2016

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research Phase I Unit
Switzerland
CH-6864

Sponsor information

Organisation
IBSA Institut Biochimique S.A

Sponsor details
Via del Piano
PO Box 266
Pambio-Noranco
Switzerland
CH-6915

Sponsor type
Industry

ROR
https://ror.org/051tj3a26

Funder(s)

Funder type
Industry

Funder Name
IBSA Institut Biochimique S.A

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
23/03/2017

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available and will be held in the Sponsor’s database.

IPD sharing plan summary
Not expected to be made available