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Adhesion study of Flectoparin® Tissugel following plaster application

Submission date
15/12/2017

Recruitment status
No longer recruiting

Registration date
20/12/2017

Overall study status
Completed

Last Edited
19/12/2017

Condition category
Skin and Connective Tissue Diseases

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

Plain English summary of protocol

Background and study aims
Diclofenac epolamine/Heparin (DHEP-Heparin) medicated plaster (Flectoparin® Tissugel), which has been first approved in Switzerland on July the 14th, 2006, is identical to DHEP medicated plaster (Flector Tissugel®) except that during the final mixing step of the manufacture a relatively small amount of unfractionated heparin of porcine origin is added to allow for a concentration of ~28 mg (5600 I.U.) per plaster, with the active ingredient diclofenac epolamine being present at the same concentration.
Through the several clinical trials conducted to date, the heparin-containing formulation has been characterized by an improved local anti-inflammatory and analgesic activity upon plaster application to the skin and, more importantly, by an enhanced clinical effectiveness when used in patients with minor sports injuries, such as joint sprains, muscle strains and contusions, particularly in terms of a significantly more marked and rapid pain reduction. The topical application avoids a large part of the undesired secondary effects occurring after systemic administration of non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac and preserves their anti-inflammatory action at a very restricted target area on the skin. The aim of this study is to assess the Flectoparin® Tissugel adherence for the intended wear period of 24 hours.

Who can participate?
Healthy volunteers aged 18-5

What does the study involve?
DHEP-Heparin medicated plaster are applied to the skin of participants without any product reinforcement, as requested, and adhesion was assessed at equally spaced intervals (4, 8, 12, 16, 20 and 24 h) after application. In addition, adherence of a DHEP-Heparin medicated plaster reinforced through corner taping was assessed in order to evaluate any differences in adhesion between the plaster without reinforcement and the reinforced plaster.

What are the possible benefits and risks of participating?
No specific benefits for the participants are foreseen. In the literature, bioavailability data both for DHEP and for other topical diclofenac salts indicate that <10% of the applied dose reaches the blood stream. Therefore, plasma diclofenac concentrations after epicutaneous applications

are several times lower than those achieved after oral administrations On the basis of these considerations, the application of two DHEP-Heparin plasters was considered to be safe. In addition, the potential risk of transdermal absorption of heparin at systemically effective concentrations could be excluded based on results of previous studies.

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?
September 2016 to December 2016

Who is funding the study?
BSA Institut Biochimique SA (Switzerland)

Who is the main contact?
Dr Milko Radicioni

Contact information

Type(s)
Scientific

Contact name
Dr Milko Radicioni

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Additional identifiers

Protocol serial number
Study CRO-PK-16-315 - Sponsor code 16CH-FHp12

Study information

Scientific Title
Adhesion study of Flectoparin® Tissugel following plaster application in healthy volunteers

Study objectives
The study is aims to assess Flectoparin® Tissugel adherence for the intended wear period of 24 hours.

Ethics approval required

Old ethics approval format

Ethics approval(s)
1. Ethics Committee Comitato Etico Cantonale, 14/11/2016
2. Non-substantial Amendment N. 1,13/12/2016
3. The Federal Health Authorities (Swissmedic), 06/12/2016: non-substantial Amendment 06/01 /2017

Study design
Single-centre single-dose open-label one-period two-treatment randomised adhesion assessment study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
The study consists of a screening visit, a treatment phase of one study period and a final visit /early termination visit (ETV).
For each subject, two DHEP-Heparin medicated plasters are applied concurrently as follows: one plaster without reinforcement (PW) and one plaster with reinforcement (PR) are applied to the right and left side of the upper back (dorsal region, below the scapula), with the longer side parallel to the spine, at the same height, as near as possible to the spine. Plaster for PR treatment was reinforced using small pieces of tape applied to the four corners of the DHEP-Heparin plaster.

The investigator assesses each plaster adhesion at 4, 8, 12, 16, 20 and 24 h post-application using the following 5-point scale, according to the FDA Guidance for Assessing adhesion.

In addition, at each time point, when adhesion was assessed on the 5-point scale, the actual percentage adherence value (%) was estimated by the investigator and reported in the CRF.

The two assessments (score and actual percentage evaluation) are visually performed by a an experienced and trained scorer (the Principal Investigator) who was previously involved as investigator in several clinical trials where visual evaluation of patch detached area was part of study assessments.

Standardised digital photographs are taken before application and at each assessment time for each plaster.

After adhesion assessment and photograph, at each assessment time the shapes of attachment /detachment area of each plaster were traced on an acetate sheet in order to collect an additional image of the detached area of each plaster.

Each plaster contained 181 mg DHEP corresponding to 140 mg diclofenac sodium. Therefore, the subjects are exposed to a total dose of approximately 280 mg diclofenac sodium.

The randomisation list is computer-generated by the Department of Biometry at the Contract Research Organization (CRO) using the PLAN procedure of the validated SAS for Windows Version 9.1.3 Service Pack 4, and supplied to the study site prior to study start.

Intervention Type
Drug

Primary outcome(s)
Adhesion score for the investigational plaster without reinforcement (PW) is measured the 5-point scale at 4, 8, 12, 16, 20 and 24 h post-application.

Key secondary outcome(s))
Safety and general tolerability of the IMP were based on the following assessments:
Record of adverse events
Adverse events (AEs) were assessed throughout the study.

Vital signs
Subjects' blood pressure and heart rate were measured by the investigator or his deputy after 5 min at rest in the sitting position at screening, on days 1-2 at pre-dose and 24 h post-application, and in case of ETV. The vital signs measurement at 24 h post-dose was considered as the final assessment.

Electrocardiograms
A 12-lead resting ECG was performed in supine position at screening and interpreted by the investigator.

Physical examination and body weight
A physical examination was performed at screening .Body weight, height and body mass index (BMI) were recorded at screening only. Subjects were weighed (kg) lightly clothed without shoes. BMI was calculated as weight [kg] / (height [m] squared).

Laboratory analysis
1. Routine haematology, blood chemistry and urinalysis laboratory tests were performed, under fasting conditions, at screening.
2. Haematology: leukocytes and leukocyte differential count (percentage and absolute values), erythrocytes, haemoglobin (conv. units), haemoglobin (IS units), haematocrit, MCV, MCH, MCHC, thrombocytes.

Blood Chemistry:
1. Electrolytes: sodium, potassium, calcium, chloride, inorganic phosphorus
2. Enzymes: alkaline phosphatase, γ-GT, AST, ALT
3. Substrates/metabolites: total bilirubin, creatinine, fasting glucose, urea, uric acid, total cholesterol, triglycerides
Proteins: total proteins

Serum pregnancy test (women only, at screening)

Urine analysis:
1. Urine chemical analysis (stick): pH, specific weight, appearance, colour, nitrites, proteins, glucose, urobilinogen, bilirubin, ketones, haematic pigments, leukocytes
2. Urine sediment (analysis performed only if positive): leukocytes, erythrocytes, flat cells, round

cells, crystals, cylinders, mucus, bacteria
3. Urine pregnancy test (women only, on day -1).
4. erum virology: Hepatitis B (HBs antigen), Hepatitis C (HCV Antibodies), HIV 1/2 (HIV Ag/Ac combo).
A urine drug test was performed at the clinical centre at screening, using a urine multi-drug kit. The following drugs were assessed: cocaine, amphetamine, methamphetamine, cannabinoids (delta-9-tetrahydrocannabinol - THC), opiates and ecstasy.

Measurements of Primary and secondary variables
Primary variables:
Adhesion scores on a 5-point numerical scale (13), where score 0=≥90% adhered (essentially no lift off the skin), score 1=≥75% to <90% adhered (some edges only lifting off the skin), score 2=≥50% to <75% (less than half of the plaster lifting off the skin), score 3=>0% to <50% adhered (not detached, but more than half of the plaster lifting off the skin without falling off), score 4=0% adhered (plaster detached; completely off the skin) for PW.

Secondary variables:
1. Adhesion scores on the 5-point numerical scale, as detailed above, for PR application.
2. Assessment of plaster adherence as a percentage of total plaster area for both PW and PR application
3. Safety variables: treatment-emergent adverse events, vital signs (blood pressure, heart rate), laboratory parameters

Completion date
21/12/2016

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and Age: 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 must be using 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 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 are admitted. For all female subjects, pregnancy test result had to be negative at screening and at each scheduled evaluation.

Participant type(s)

Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
55 years

Sex
All

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. Application site: diseased-skin, skin wounds or open injuries at the applications site
7. 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
8. 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 follows the last visit of the previous study and the first day of the present 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 2015-2020], 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
12/12/2016

Date of final enrolment
14/12/2016

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research Phase I Unit
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Sponsor information

Organisation
IBSA Institut Biochimique SA

ROR
https://ror.org/051tj3a26

Funder(s)

Funder type
University/education

Funder Name
IBSA Institut Biochimique SA

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository at CRO site.

IPD sharing plan summary
Stored in repository