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Study to evaluate the adhesion and bioavailability of Diclofenac 2.6% medicated plaster in healthy volunteers

Submission date
27/05/2022

Recruitment status
No longer recruiting

Registration date
13/06/2022

Overall study status
Completed

Last Edited
07/12/2022

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Diclofenac is a non-steroidal anti-inflammatory drug (NSAID). NSAIDs are widely used to reduce inflammation and pain in patients suffering from arthritis and other painful conditions secondary to trauma (i.e. minor sport injuries) or rheumatic diseases. The same drug orally administered is known to have the potential of severe gastrointestinal side effects while topical application to the skin usually does not show any adverse effects affecting the whole body.

Several studies performed on hundreds of patients have previously shown the safety and the clinical efficacy of plasters containing Diclofenac 1.3%. A new plaster containing a higher concentration of Diclofenac (2.6%) has been recently developed with the aim of improving its anti-inflammatory efficacy and improving the frequency of patients using the plaster.

The study aims to evaluate the adhesion (sticking) of the plaster and diclofenac levels in the blood. Data on how well participants tolerate the plaster will also be collected. Furthermore, the rate and extent to which the medication in the plaster is absorbed and reaches the blood, as well as the amount of the breakdown products of the medication in the blood, will be studied. Finally safety data will be collected.

Who can participate?
Healthy volunteers aged between 45 and 65 years inclusive

What does the study involve?
For each participant, two medicated plasters will be applied at the same time to the front part of each leg, in a horizontal position, just below the knee. One of two plasters will be reinforced. The method used to reinforce the plaster will be chosen at random, either with an elastic net or with 4 surgical tapes applied to the 4 medicated plaster corners. The other plaster will be applied without reinforcement. The leg on which the reinforced plaster will be placed will be chosen at random for each participant. The two plasters will be applied in the morning , once a day for 5 days and will be kept in place for 24 h.

What are the possible benefits and risks of participating?
No potential benefits are foreseen to subjects participating in this study.
Over a million patients have been treated with diclofenac as a medicated plaster since its first registration. No relevant risks have emerged related to exposure to the medicinal product, with any unwanted effects limited mainly to the site of products' application.

Where is the study run from?
CROSS Research S.A. Phase I Unit Clinical Centre (Switzerland)

When is the study starting and how long is it expected to run for?
From July 2021 to October 2021

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

Who is the main contact?
Carol Caverzasio, sd@ibsa.ch

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Additional identifiers

Protocol serial number
CRO Code: CRO-PK-21-354 - Sponsor Code: 20CH-Fpf08

Study information

Scientific Title
Adhesion and bioavailability study of a new DHEP 2.6% medicated plaster following repeated applications in healthy male and female volunteers

Acronym
DHEP 2.6%

Study objectives
Evaluation of adhesion and plasma diclofenac pharmacokinetic profile of DHEP 2.6% medicated plaster in healthy male and female volunteers after repeated applications for 5 consecutive days.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/08/2021, Ethic Committee of Canton Ticino (c/o Ufficio di sanità, Via Orico 5 6501 Bellinzona; +41 (0)8143057; michaela.gutacker@ti.ch), ref: 2021-01530 CE TI3926

Primary study design
Interventional

Study design
Single center, repeated application, open label, randomized, adhesion and bioavailability study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
DHEP 2.6% medicated plasters for analgesia and anti-inflammatory effects

Interventions
For each subject, two DHEP 2.6% medicated plasters (one plaster with reinforcement [PR] and one plaster without reinforcement [PW]) will be applied concurrently to the anterior part of each leg, in horizontal position, just below the knee. Half of the plasters for PR treatment will be reinforced with an elastic net (PRN) and half with 4 surgical tapes applied to the 4 medicated plaster corners (PRT). Each subject will receive PW on one leg (right or left) and either PRN or PRT on the other leg (right or left) according to the study randomization list. The randomization list will be computer-generated by the Biometry Unit of the Clinical Contract Research Organization (CRO), using the PLAN procedure of the SAS® version 9.3 (TS1M1). The randomization list will be supplied to the study site before the study start. The randomization list will be attached to the final clinical study report (CSR).

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Diclofenac N(2-hydroxyethyl)-pyrrolidine (DHEP) 2.6%

Primary outcome(s)
1. Adhesion measured using adhesion scores on a 5-point scale and estimated percentage of adhered plaster area for DHEP 2.6% medicated plaster applied with and without reinforcement at 4, 8, 12, 16, 20, and 24 h post-application
2. Bioavailability of Diclofenac measured using Cmax0-24h, C24h, AUC 0-24h, tmax 0-24h, Cmin 0-24h, C ave0-24h, and Flu% (0-24h) of diclofenac in plasma after repeated applications of DHEP 2.6% medicated plaster calculated using the validated software Phoenix WinNonlin® version 6.3 from plasma samples collected at pre-application (0 h) on days 1-4, and at pre-application (0 h) and 0.5, 1, 2, 3, 4, 6, 9, 12, 14, 16, and 24 h post-application at 5 days

Key secondary outcome(s)
1. Safety measured using:
1.1. The incidence of treatment-emergent adverse events collected throughout the study
1.2. Vital signs:
1.2.1. Blood pressure measured after 5 min at rest in the sitting position using a sphygmomanometer at screening, -1 day, and at 24 h post-application at 5 days
1.2.2. Heart rate measured after 5 min at rest in the sitting position using pulse rate at screening, -1 day, and at 24 h post-application at 5 days
1.2.3. Local tolerability measured using clinical assessment and rating of the erythema, dryness, swelling, and exfoliation at the plaster application site on a 4-grade scale at pre-application (0 h) on day 1 and immediately after plaster removal at 2, 3, 4, 5, and 6 days
1.2.4. Physical examinations measured using overall Investigator’s interpretation and clinically significant abnormalities) at the screening and final visit/ETV

1.2.5. Body weight measured using scales at screening and final visit/ETV
1.2.6. Laboratory parameters of hematology (leukocytes and leukocyte differential count, erythrocytes, hemoglobin, hematocrit, MCV, MCH, MCHC, thrombocytes); blood chemistry; electrolytes (sodium, potassium, calcium, chloride, inorganic phosphorus); enzymes (alkaline phosphatase, γ-GT, AST, ALT); substrates/metabolites (total bilirubin, creatinine, glucose, urea, uric acid, total cholesterol, triglycerides); proteins (total proteins); serum virology (Hepatitis B [HBs antigen], Hepatitis C [HCV antibodies], HIV 1/2 [HIV Ag/Ab combo]); urine chemical analysis (pH, specific weight, appearance, color, nitrites, proteins, glucose, urobilinogen, bilirubin, ketones, hematic pigments, leukocytes); and urine sediment analysis (leukocytes, erythrocytes, flat cells, round cells, crystals, cylinders, mucus, bacteria) measured from blood and urine samples collected at screening

If feasible, the following will also be measured:
1. Bioavailability of epolamine and epolamine N-O measured using Cmax0-24h, C24h, AUC0-24h, tmax0-24h, Cmin0-24h, Cave0-24h, and Flu% (0-24h) of epolamine and epolamine N-O in plasma after repeated applications of DHEP 2.6% medicated plaster calculated using the validated software Phoenix WinNonlin® version 6.3 from plasma samples collected on Days 1-4 at pre-application (0), and on Day 5 at pre-application (0) and at 0.5, 1, 2, 3, 4, 6, 9, 12, 14, 16, and 24 h post-application

Completion date
28/10/2021

Eligibility

Key inclusion criteria
1. Signed written informed consent before inclusion in the study
2. Men or women aged between 45 and 65 years inclusive
3. Body Mass Index (BMI) between18.5 and 30 kg/m² inclusive
4. Vital signs measured after 5 min at rest in the sitting position:
4.1. Systolic blood pressure (SBP) 100-139 mmHg
4.2. Diastolic blood pressure (DBP) 50-89 mmHg
4.3 Heart rate 50-90 bpm
5. Able 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. Women 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 (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 agrees to use a male condom with spermicide
6.4. A sterile sexual partner.
7. Women of non-child-bearing potential or in post-menopausal status for ≥1 year
8. Negative pregnancy test result at screening and Day -1.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
45 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
24

Key exclusion criteria
1. Clinically significant abnormalities on 12-lead (supine position) electrocardiogram (ECG)
2. Clinically significant abnormal physical findings which could interfere with the objectives of the study
3. Clinically significant abnormal laboratory values indicative of physical illness
4. Diseased skin, skin wounds, open injuries or tattoos at the application site or any other physical/medical condition which could interfere with the objectives of the study
5. Known or presumed hypersensitivity to the active principle and/or formulations' ingredients
6. History of anaphylaxis to drugs or allergic reactions in general, which the Investigator considers may affect the outcome of the study
7. Significant history of renal, hepatic, gastrointestinal, cardiovascular, respiratory, skin, hematological, endocrine or neurological diseases that may interfere with the aim of the study
8. Medications, including over the counter (OTC) medications (in particular, non-steroidal anti-inflammatory drugs) and herbal remedies, used within the 2 weeks before the start of the study. Hormonal contraceptives for women will be allowed.
9. Participation in the evaluation of any investigational product within the 3 months before this study. The 3-month interval is 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.
10. Blood donations within the 3 months before this study
11. History of drug, alcohol (>1 drink/day for women and >2 drinks/day for men, defined according to the USDA Dietary Guidelines 2020-2025), caffeine (>5 cups coffee/tea/day), or tobacco abuse (≥10 cigarettes/day)
12. Positive result at the drug test at screening or Day -1
13. Positive alcohol breath test at Day -1
14. Abnormal diets (<1600 or >3500 kcal/day), vegetarian diet, or substantial changes in eating habits in the 4 weeks before this study
15. Positive or missing pregnancy test at screening or Day -1
16. Pregnant or lactating

Date of first enrolment
11/10/2021

Date of final enrolment

21/10/2021

Locations

Countries of recruitment
Switzerland

Study participating centre
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Sponsor information

Organisation
IBSA Institut Biochimique S.A.

Funder(s)

Funder type
Industry

Funder Name
IBSA Institut Biochimique S.A.

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			14/11/2022	No	No