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Bioavailability and tolerability study of two new diclofenac epolamine lecithin gel formulations (2.6% and 3.9%) in comparison with the marketed diclofenac epolamine lecithin gel formulation 1.3% (Effigel® IBSA)

Submission date
15/05/2017

Recruitment status
No longer recruiting

Registration date
16/05/2017

Overall study status
Completed

Last Edited
16/05/2017

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
Diclofenac is an anti-inflammatory painkiller that can be applied as a gel. Two new gel formulations have been developed that contain higher amounts of diclofenac (2% and 3%) compared to the approved gel formulation, Effigel (1%). This may improve the painkilling/anti-inflammatory effect by increasing the amount of diclofenac at the application site while keeping levels in the rest of the body very low to avoid side effects. Higher strength gels could also be applied less often. The aim of this study is to measure the levels of diclofenac in the blood and the side effects after applying each of the gels.

Who can participate?
Healthy volunteers aged 18-55

What does the study involve?
There are three study periods separated by breaks of at least 5 days. In each period participants are treated with one of the three diclofenac gels, divided into two daily 8 g applications. Each dose of gel is applied to the maximum area of skin recommended for Effigel (800 cm2). For the 30 minutes after each application participants remain seated and the application area is kept naked. Blood levels of diclofenac are measured by taking 13 blood samples over the course of the following 12 hours. During these 12-hour periods participants stay in the trial centre and hazardous, strenuous or athletic activities are not permitted. Side effects and vital signs (blood pressure, heart rate) are measured and physical examinations and laboratory tests are performed at the start and the end of the study.

What are the possible benefits and risks of participating?
No specific benefits for the participants are foreseen. The safety of Effigel has already been confirmed. Blood diclofenac levels after skin applications are much lower than those reached

when diclofenac is taken orally. No significant risks related to Effigel® have been reported - the side effects most frequently reported are mild-moderate skin reactions where the gel is applied. No other significant risks are expected for the participants.

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?
January to June 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

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Additional identifiers

Protocol serial number
CRO-PK-15-309 - Sponsor code 16CH-Fgf01

Study information

Scientific Title
Bioavailability and tolerability study of two new diclofenac epolamine lecithin gel formulations (2.6% and 3.9%) in comparison with the marketed diclofenac epolamine lecithin gel formulation 1.3% (Effigel® IBSA): an open-label three-way randomised cross-over pilot bioavailability study

Study objectives
Evaluate the plasma diclofenac pharmacokinetics and the safety and tolerability in healthy subjects after two consecutive applications of two new gels containing ascending concentrations of diclofenac epolamine (DHEP), 2.6% (test 1, T1) and 3.9% (test 2, T2), in

comparison with the marketed reference Effigel®, gel containing DHEP at the concentration of 1.3% (R).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Comitato Etico Cantonale, Canton Ticino, Switzerland, 22/03/2016, ref: CE3042, BASEC (Business Administration System for Ethics Committee) 2016-00346

Study design
Open-label three-way randomised cross-over pilot bioavailability study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Bioavailability and tolerability study of two new diclofenac epolamine lecithin gel formulations

Interventions
The study consisted of a screening visit, a treatment phase of three study periods separated by wash-out intervals of at least 5 days between the start of the 2nd application of a period and the start of the 1st application of the following period, and a final visit/early termination visit.

Test 1 (T1): DHEP 2.6% (corresponding to 2% of diclofenac sodium) gel, IBSA Institut Biochimique S.A.,Switzerland. Batch N. 160101, re-test date JUL16
Test 2 (T2): DHEP 3.9% (corresponding to 3% of diclofenac sodium) gel, IBSA Institut Biochimique S.A.,Switzerland. Batch N. 160102, re-test date JUL16
Reference (R): Effigel®, DHEP 1.3% (corresponding to 1% of diclofenac sodium) gel, IBSA Institut Biochimique S.A., Switzerland. Batch N. 150606, expiry date JUN18

Each subject received a total of 16 g of each IMP. The total dose was subdivided into two applications of 8 g each. Considering the dose regimen of up to four daily applications recommended for Effigel®, two daily applications of 8 g each were tested in the present study. Each dose of 8 g of gel was applied to the maximum application area (800 cm2) as recommended for Effigel®.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Diclofenac

Primary outcome(s)

Pharmacokinetic parameters (Cmax, AUC0-t, AUC0-∞, t1/2, λz and tmax) of plasma diclofenac free acid after two applications of T1, T2 and R. Plasma concentrations of diclofenac are measured at the following time-points (13 samples in each study period):
1. On day 1 at pre-dose (0), i.e. before the start of the 1st application
2. On day 2 at pre-dose (0), i.e. 5 min before the start of the 2nd application, and at 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 10, 12 h after the start of the 2nd application

Key secondary outcome(s))
1. Treatment-emergent adverse events; vital signs (blood pressure, heart rate); physical examinations and laboratory tests performed at screening and final visit/early termination visit
2. Local tolerability, evaluated according to a 4-grade score scale before the start and 2 h after the start of the 1st application and before the start and 4 and 12 h after the start of the 2nd application

Completion date
30/06/2016

Eligibility

Key inclusion criteria
1. Signed written informed consent
2. Males/females, 18-55 year old inclusive
3. Body Mass Index (BMI): 18.5-30 kg/m2 inclusive
4. Vital signs: systolic blood pressure 100-139 mmHg, diastolic blood pressure 50-89 mmHg, heart rate 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 (women only): women 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 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 day 1

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. 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 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 (women only): positive or missing pregnancy test at screening or day 1, pregnant or lactating women

Date of first enrolment
02/05/2016

Date of final enrolment
06/05/2016

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research Phase I Unit
CH-6864

Sponsor information

Organisation
IBSA Institut Biochimique S.A

ROR
https://ror.org/051tj3a26

Funder(s)

Funder type
Industry

Funder Name
IBSA Institut Biochimique S.A

Results and Publications

Individual participant data (IPD) sharing plan
The investigator and the CRO will ensure that all raw data records, medical records, CRFs and all other documentation that is relevant to this study will be made accessible for monitoring activities, audits, IEC review, and regulatory inspections.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes