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Comparative bioavailability of diclofenac epolamine tablets vs. Flector® granules for oral solution in healthy volunteers, pilot study in fed conditions

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Registration date 10/11/2017	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 09/11/2017	**Condition category** Other	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
The aim of this study is to compare the bioavailability (blood levels) of diclofenamic acid after taking a new diclofenac epolamine 50 mg tablet formulation (65 mg of diclofenac epolamine corresponding to 50 mg of diclofenac sodium), compared with the market reference Flector® granules for oral solution, 50 mg sachets (65 mg of diclofenac epolamine corresponding to 50 mg of diclofenac sodium), taken in a single dose under fed conditions by healthy volunteers.

Who can participate?
Healthy men aged 18-55

What does the study involve?
Participants are randomly allocated to take one of the two treatments (either a diclofenac epolamine tablet or Flector® granules) during period 1 and the other treatment during period 2, with a break of at least 5 days between the periods. The blood level of diclofenamic acid is measured pre-dose (0) and 3, 9, 15, 21, 30, 45 min, 1, 1.25, 1.5, 2, 3, 4, 6 and 8 h after the dose.

What are the possible benefits and risks of participating?
No specific benefits for the participants are foreseen

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?
February 2017 to May 2017

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

Who is the main contact?
Dr Milko Radicioni

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
Study CRO-PK-16-312 - Sponsor code 16CH-GIB04

Study information

Scientific Title
Comparative bioavailability of diclofenac epolamine tablets vs. Flector® granules for oral solution in healthy volunteers, pilot study in fed conditions

Study objectives
This study aimed to obtain predictive data of the pharmacokinetic profile of the test formulation (Diclofenac epolamine [DHEP] 50 mg soluble tablets, containing 65 mg of diclofenac epolamine corresponding to 50 mg of diclofenac sodium) in comparison with the reference product (Flector® EP granulé) when administered in fed conditions before performing a pivotal bioequivalence study and, if necessary, to improve the test product composition until an optimal formulation is reached.
Although the test product was designed aiming to display a rapid release profile and similarity towards the formulation in granules was showed in the previous studies, the impact of food on the pharmacokinetics (PK) of the two formulations was never investigated.
A pilot study was therefore deemed a reasonable choice in order to avoid the repetition of pivotal studies and the exposure of an excessive number of volunteers both to the test and to the reference products.
The study has been designed according to EMA guidelines on the investigation of bioavailability and bioequivalence.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Comitato Etico Cantonale, Canton Ticino, Switzerland, 19/07/2016, ref: 3085 – Based 2016-01097. The Federal Health Authorities (Swissmedic) assigned the reference number 2016DR1177 to the study on 01/12/2016.

Study design
Single-centre single-dose open randomised two-way cross-over bioavailability pilot study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diclofenac epolamine (DHEP) 50 mg soluble tablets containing 65 mg of diclofenac epolamine corresponding to 50 mg of diclofenac sodium

Interventions
Test product (T): Diclofenac epolamine (DHEP) 50 mg soluble tablets containing 65 mg of diclofenac epolamine corresponding to 50 mg of diclofenac sodium
Reference therapy (R): Flector® granules for oral solution, 50 mg sachets containing 65 mg of diclofenac epolamine corresponding to 50 mg of diclofenac sodium

A single dose of T and R was administered to healthy male volunteers under fed conditions according to a randomised two-way cross-over design, with a wash-out interval of at least 5 days between consecutive administrations. The subjects were assigned to one sequence of treatments (TR or RT) according to the randomisation list and the cross-over design. The subjects were randomised to receive one of the two treatments (i.e. either T or R) during period 1 and the other treatment during period 2.

The concentration of diclofenamic free acid in plasma was measured at the following time-points: pre-dose (0) and 3, 9, 15, 21, 30, 45 min, 1, 1.25, 1.5, 2, 3, 4, 6 and 8 h post-dose.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Rate (Cmax) and extent (AUC0-t) of absorption of diclofenamic acid: the concentration of diclofenamic free acid in plasma was measured at the following time-points: pre-dose (0) and 3, 9, 15, 21, 30, 45 min, 1, 1.25, 1.5, 2, 3, 4, 6 and 8 h post-dose

Key secondary outcome(s))
1. Pharmacokinetic (PK) profile of diclofenamic acid: the concentration of diclofenamic free acid in plasma was measured at the following time-points: pre-dose (0) and 3, 9, 15, 21, 30, 45 min, 1,

1.25, 1.5, 2, 3, 4, 6 and 8 h post-dose
2. Safety and tolerability of diclofenamic acid:
2.1. Record of adverse events: AEs assessed throughout the study
2.2. Vital signs: subjects' blood pressure (BP) and heart rate (HR) measured by the investigator or his/her deputy after 5 min at rest in sitting position at: screening visit, day 1 of each period: pre-dose (0) and 8 h post-dose, ETV. The check on day 1, 8 h post-dose of period 2, also corresponded to the final assessment
2.3. Electrocardiograms: a 12-lead resting ECG performed and interpreted by the investigator at the screening and final visit
2.4. Physical examination, performed at screening and at final visit. Body weight (BW) recorded at screening and at final visit. Subjects weighed (kg) lightly clothed without shoes
2.5. Height and Body Mass Index (BMI) recorded at screening visit. BMI calculated as weight [kg] / (height [m] squared)
2.6. Laboratory analysis: routine haematology, blood chemistry and urinalysis laboratory tests performed under fasting conditions at screening
2.7. A urine drug test performed using a urine multi-drug kit at screening. The following drugs assessed: cocaine, amphetamine, methamphetamine, cannabinoids (delta-9-tetrahydrocannabinol - THC), opiates and ecstasy. The same analyses, with the exception of drug screening and virology, performed at the final visit

Completion date
15/05/2017

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and age: males, 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

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
55 years

Sex

Male

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

Date of first enrolment
02/05/2017

Date of final enrolment
02/05/2017

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research Phase I Unit
Via F. A. Giorgioli 14
6864

Sponsor information

Organisation
IBSA Institut Biochimique SA

ROR
https://ror.org/051tj3a26

Funder(s)

Funder type
Industry

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 publically available repository.

IPD sharing plan summary
Stored in repository