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

Submission date	Recruitment status	<ul><li>Prospectively registered</li></ul>
09/11/2017	No longer recruiting	Protocol
Registration date	Overall study status	Statistical analysis plan
10/11/2017	Completed	Results
Last Edited	Condition category	[] Individual participant data
09/11/2017	Other	<ul><li>Record updated in last year</li></ul>

# 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)

# Contact information

# Type(s)

Scientific

### Contact name

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### Contact details

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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: predose (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

# 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**

# **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

# **Study outputs**

Output type Details Date created Date added Peer reviewed? Patient-facing?

Participant information sheet
Participant information sheet
11/11/2025 No
Yes