

# Study to assess the distribution in healthy male volunteers' blood and urine of one and two consecutive doses of the antibiotic fosfomycin

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| <b>Submission date</b><br>22/03/2022   | <b>Recruitment status</b><br>No longer recruiting | <input type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol                       |
| <b>Registration date</b><br>25/03/2022 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input type="checkbox"/> Results                       |
| <b>Last Edited</b><br>25/03/2022       | <b>Condition category</b><br>Other                | <input type="checkbox"/> Individual participant data<br><input type="checkbox"/> Record updated in last year |

## Plain English summary of protocol

### Background and study aims

Fosfomycin is a widely used antibiotic for urinary tract bacterial infections and has been shown to prevent infectious complications in patients after undergoing urological procedures, such as surgical and transurethral diagnostic procedures and transrectal prostate biopsy, which are commonly performed to diagnose prostatic carcinoma (prostate cancer). The sponsor designed the present study to get more information in healthy male volunteers about fosfomycin concentrations in blood, urine and the male genital tract and its safety of use after two doses (one dose of 3 g fosfomycin given 3 hours before surgery and a second dose of 3 g given 24 hours after surgery), which is currently used in the above-mentioned urological procedures.

### Who can participate?

Healthy men volunteers aged 40-70 years

### What does the study involve?

All participants receive the following treatment: one dose of 3 g of fosfomycin (as fosfomycin trometamol) on Day 1, at 07:00 ± 1 h under fasting conditions and one dose of 3 g of fosfomycin (as fosfomycin trometamol) on Day 3 at 07:00 ± 1 h under fasting conditions followed by a second dose of 3 g of fosfomycin (as fosfomycin trometamol) exactly 27 h later, that is on Day 4, at 10:00 ± 1 h. During the study, blood, urine and seminal plasma samples are collected from participants for the measurement of fosfomycin in the bloodstream, urine and seminal plasma and of fructose and PSA in seminal plasma. Heart rate and blood pressure are measured, ECG is recorded and blood and urine laboratory tests are performed to test the safety of the medication.

### What are the possible benefits and risks of participating?

No specific benefits for the study participants are foreseen. Their remuneration is paid after study completion. The remuneration covers loss of time and any inconvenience caused by the participation in the study. No particular risks are expected for the study subjects originating from the scheduled fosfomycin dose regimen, considering that fosfomycin trometamol is a well-known drug which has been used for decades. The safety of the drug is generally good. A few

undesired effects have been commonly (at a frequency  $\geq 1/100$  and  $< 1/10$ ) reported: diarrhoea, nausea, dyspepsia, headache and dizziness. Blood sampling with cannula insertion may cause minor discomfort. The risks associated with blood draws include pain, bleeding and bruising.

Where is the study run from?

Zambon S.p.A. (Italy)

When is the study starting and how long is it expected to run for?

December 2020 to September 2021

Who is funding the study?

Zambon S.p.A. (Italy)

Who is the main contact?

Dr Maria Constanza Oliveros Celis  
Global Head Medical Affairs and Patient's Advocacy  
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## Contact information

### Type(s)

Scientific

### Contact name

Dr Maria Constanza Oliveros Celis

### Contact details

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## Additional identifiers

### Protocol serial number

CRO-PK-20-349, sponsor code Z7215J01

## Study information

### Scientific Title

Pharmacokinetic study of one and two consecutive doses of oral fosfomycin trometamol in healthy male volunteers

### Study objectives

To evaluate fosfomycin concentrations and pharmacokinetics (PK) in plasma and urine in healthy men after one and two consecutive doses of the investigational medicinal product (IMP).

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Approved 08/02/2021, Cantonal Ethics Committee Canton Ticino (c/o Health Office, Via Orico 5, 6501 Bellinzona, Switzerland; +41 (0)91 8143057; dss-ce@ti.ch), ref: CE 3796, BASEC 2020-03039

## Study design

Single- and multiple-dose single-centre open-label one-way pharmacokinetics, safety and tolerability Phase I clinical study

## Primary study design

Interventional

## Study type(s)

Other

## Health condition(s) or problem(s) studied

Pharmacokinetic study in healthy male volunteers

## Interventions

All the subjects enrolled in the study receive the same treatment with the investigational medicinal product (IMP) as follows:

1. On Day 1, one dose of 3 g of fosfomycin (as fosfomycin trometamol) is administered under fasting conditions at 07:00 ± 1 h.

After a wash-out of exactly 48 h:

2. On Day 3, one dose of 3 g of fosfomycin (as fosfomycin trometamol) is administered under fasting conditions at 07:00 ± 1 h, followed by a second dose of 3 g of fosfomycin (as fosfomycin trometamol) exactly 27 h later, on Day 4, at 10:00 ± 1 h.

At each dosing, the entire content of one sachet of IMP is dispersed until complete dissolution in 75 ml of still mineral water and drunk by the subject. Afterwards, the glass is rinsed with a further 50 ml of still mineral water and the rinse drunk.

This is a non-randomised study. All the subjects receive the same study treatment.

During the interventional phase, blood samples are collected for PK analysis at pre-dose (0), 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 10, 12, 16, 24, 30 and 36 h post-dose. Urine is collected during the following time intervals on Days 1-2, after the single dose, and on Days 4-5, after the second multiple dose: 0-4, 4-8, 8-12, 12-16, 16-24 and 24-36 h post-dose.

Together with blood and urine, also the seminal plasma is collected for PK analysis. In detail, the subjects are instructed to masturbate and ejaculate their semen at about 2.5 h post-dose on Day 1, after the single dose, and Day 4, after the second multiple dose, and in any case, before the 2.5-h post-dose blood sampling. They are instructed to collect their semen into a five-compartment plastic collection tray in a single pass across the long axis of the tray. Each sample is processed for the determination of the concentration of fosfomycin in plasma, urine and seminal plasma. Seminal plasma is analysed also to determine the concentration of fructose and

PSA. Safety and general tolerability of the IMP are based on adverse events, ECG, physical examinations including body weight, vital signs and routine haematology, blood chemistry and urinalysis laboratory tests.

## **Intervention Type**

Drug

## **Phase**

Phase I

## **Drug/device/biological/vaccine name(s)**

Monuril® (fosfomycin trometamol)

## **Primary outcome(s)**

Fosfomycin concentrations and pharmacokinetics evaluated in plasma and urine using a fully validated liquid chromatography with tandem mass spectrometry (LC-MS-MS) method after one dose (Day 1) and two consecutive doses (Day 4) of the investigational medicinal product

## **Key secondary outcome(s)**

1. Fosfomycin concentrations evaluated in prostate and seminal vesicles using a fully validated liquid chromatography with tandem mass spectrometry (LC-MS-MS) method after one dose (Day 1) and two consecutive doses (Day 4) of the investigational medicinal product
2. Safety and tolerability of the treatment evaluated by collecting the adverse events during the whole study and measuring vital signs (blood pressure and heart rate) at screening, on Days 1-2 and Days 4-5 and at the final visit. Safety and tolerability of the treatment are also evaluated by measuring the laboratory parameters, performing physical examinations including body weight and registering the ECG at screening and the final visit.

## **Completion date**

08/09/2021

# **Eligibility**

## **Key inclusion criteria**

1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and age: men, 40-70 years old inclusive
3. Body Mass Index (BMI): 18.5-30 kg/m<sup>2</sup> inclusive
4. Vital signs: systolic blood pressure (SBP) 100-139 mmHg, diastolic blood pressure (DBP) 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 study

## **Participant type(s)**

Healthy volunteer

## **Healthy volunteers allowed**

No

## **Age group**

Adult

**Lower age limit**

18 years

**Sex**

Male

**Total final enrolment**

24

**Key exclusion criteria**

1. Electrocardiogram (ECG) 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 considers may affect the outcome of the study
5. Diseases: significant history of renal, hepatic, gastrointestinal, cardiovascular, respiratory, genitourinary, skin, haematological, endocrine or neurological diseases that may interfere with the aim of the study
6. Medications: medications, including over the counter (OTC) medications and herbal remedies for 2 weeks before the screening visit
7. Investigative drug studies: participation in the evaluation of any investigational product for 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
8. Blood donation: blood donations for 3 months before this study
9. Drug, alcohol, caffeine, tobacco: history of drug, alcohol [ $>2$  drinks/day, defined according to the USDA Dietary Guidelines 2015], caffeine ( $>5$  cups coffee/tea/day) or tobacco abuse ( $\geq 10$  cigarettes/day)
10. Drug test: positive result at the drug test at screening or day -1
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

**Date of first enrolment**

18/03/2021

**Date of final enrolment**

12/04/2021

**Locations**

**Countries of recruitment**

Switzerland

**Study participating centre**  
CROSS Research S.A. - Phase I Unit  
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6864

## Sponsor information

**Organisation**  
Zambon (Italy)

**ROR**  
<https://ror.org/04zzq8d03>

## Funder(s)

**Funder type**  
Industry

**Funder Name**  
Zambon S.p.A.

## Results and Publications

### Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date.

### IPD sharing plan summary

Data sharing statement to be made available at a later date