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Study to evaluate the amount of ketoprofen remaining in the mouth and its concentration in saliva after mouthwash rinse with OKI gola® 1.6% collutorio in healthy male and female volunteers

Submission date	Recruitment status	[ ] Prospectively registered
13/05/2022	No longer recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
24/05/2022	Completed	[ ] Results
Last Edited	Condition category	[ ] Individual participant data
23/05/2022	Other	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The Dompé formulation of ketoprofen lysine salt (KLS) for oropharyngeal use (Oki Gola® 1,6% mouthwash) has been developed to provide a more convenient and alternative treatment to currently marketed topical anaesthetic or anti-inflammatory preparations. Over systemic administration of KLS, this formulation presents the advantage of reaching the inflamed area directly through a targeted application to the site where the inflammatory process is developing and limiting the drug spreading to other regions of the body.
The Oki Gola® 1,6% mouthwash presentation consists of an aqueous solution of ketoprofen lysine salt at a 1.6% concentration, marketed in a 150 mL plastic bottle package with a child-proof closure and a 10 mL measuring cap.
Oki Gola® 1,6% mouthwash is indicated for the symptomatic treatment of irritative and inflammatory conditions of the oropharynx (such as gingivitis, stomatitis, pharyngitis), even associated with pain, and also as a consequence of preventive or extractive dental therapy.
The sponsor has designed the present study to get more information from healthy volunteers about the amount of ketoprofen remaining in the oral cavity and the salivary concentrations of ketoprofen after 3 mouthwash rinses with the product.

Who can participate?
Healthy male and female volunteers aged 18-55 years

What does the study involve?
All the subjects enrolled in the study receive the same treatment: one dose of the investigational medicinal product (IMP) administered as a mouthwash in 3 rinses, for a total dose of 160 mg of ketoprofen lysine salt.
Before each administration, 10 mL of OKI gola® 1.6% collutorio (mouthwash) are diluted to 100 mL, corresponding to a final concentration of 1.6 mg/mL ketoprofen lysine salt, using still

mineral water at room temperature. For the treatment, the subjects rinse their mouth three times with the diluted solution of OKI gola® mouthwash - about 33 mL each rinse. Each rinse lasts for at least 10 sec and afterwards, the subjects expel the liquid.
During the study, saliva and blood samples are collected from participants for the measurement of ketoprofen concentrations in saliva and in the bloodstream. Heart rate and blood pressure are measured 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.
The product safety data confirm a positive benefit/risk ratio. No particular risks are expected for the study subjects considering that the IMP is used according to the dose regimen indicated in the summary of the product characteristics. 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?
Dompé farmaceutici S.p.A., Italy

When is the study starting and how long is it expected to run for?
May 2021 to December 2021

Who is funding the study?
Dompé farmaceutici S.p.A., Italy

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
CRO-PK-21-352, Sponsor code KSL0221

Study information

Scientific Title
Single-way open label phase I study to evaluate the amount of ketoprofen remaining in the oral cavity and ketoprofen salivary concentration after mouthwash rinse with OKI gola® 1.6% collutorio in healthy volunteers of both sexes

Acronym
OKI gola® 1.6% PK

Study objectives
To determine the amount of ketoprofen remaining in the oral cavity and the salivary concentrations of ketoprofen after 3 mouthwash rinses with the investigational medicinal product.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/07/2021 and 23/07/2021, 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 3912, BASEC 2021-01378

Primary study design
Interventional

Study design
Phase I single-centre single-dose single-way open-label pharmacokinetic study

Study type(s)
Other

Health condition(s) or problem(s) studied
Phase I study in healthy volunteers of both sexes

Interventions
All the subjects enrolled in the study receive the same treatment: one dose of the investigational medicinal product (IMP - OKI gola® 1.6% collutorio) administered as mouthwash in 3 rinses, for a total dose of 160 mg of ketoprofen lysine salt. Before each administration, 10 mL of OKI gola® 1.6% collutorio (mouthwash) are diluted to 100 mL, corresponding to a final concentration of 1.6 mg/mL ketoprofen lysine salt, using still mineral water at room temperature. For the treatment, the subjects rinse their mouth three times with the diluted solution of OKI gola® mouthwash - about 33 mL each rinse. Each rinse lasts for at least 10 sec and afterwards the subjects expel the liquid.
During the study, saliva samples for ketoprofen concentrations analysis are collected at pre-

dose (0) and 1, 2, 4, 6, 10, 15, 20 and 30 min post-dose. Venous blood samples are collected from a forearm vein at pre-dose (0) and 4, 6, 10, 15, 20 and 30 min post-dose.
Safety and general tolerability of the IMP are based on adverse events, physical examinations including body weight, and vital signs.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
OKI gola® 1.6% collutorio

Primary outcome(s)
The amount of ketoprofen remaining in the oral cavity after the mouthwash rinses is measured using a fully validated HPLC-UV method. Salivary ketoprofen pharmacokinetic profile is evaluated up to 30 min post dose using the same analytical method.

Key secondary outcome(s)
1. Plasma ketoprofen pharmacokinetic profile is evaluated up to 30 min post dose using a fully validated HPLC-UV method.
2. Safety and tolerability of the study treatment are evaluated by collecting the adverse events during the whole study, by measuring vital signs (blood pressure and heart rate) at screening and final visit, and by performing a physical examination at screening and final visit.

Completion date
13/12/2021

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and age: men/women, 18-55 years old inclusive
3. Body Mass Index (BMI): 18.5-30 kg/m² inclusive
4. Vital signs: systolic blood pressure (SBP) 100-139 mmHg, diastolic blood pressure (DBP) 50-89 mmHg, pulse rate 50-90 bpm and body temperature 35.5-37.5° C, 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
6. Contraception and fertility (women only): 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 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
Women of non-child-bearing potential or in post-menopausal status for at least 1 year are

admitted.
For all women, pregnancy test result must be negative at screening.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
36

Key exclusion criteria
1. Physical findings: clinically significant abnormal physical findings which could interfere with the objectives of the study
2. Allergy: ascertained or presumptive hypersensitivity to the active principles (ketoprofen lysine salt or derivatives) and/or formulations' ingredients; known hypersensitivity to non-steroidal anti-inflammatory drugs; history of hypersensitivity to drugs (in particular to ketoprofen) or allergic reactions in general, which the Investigator considers may affect the outcome of the study
3. Diseases: significant history of renal, hepatic, gastrointestinal, respiratory, skin, haematological, endocrine, neurological or cardiovascular diseases that may interfere with the aim of the study; mouth lesions or any other oral mucosa alteration that may interfere with the aim of the study according to the investigator’s opinion
4. Medications: medications, including over the counter drugs (in particular non-steroidal anti-inflammatory drugs), mouthwashes, oral rinses, herbal remedies and food supplements taken 14 days before the start of the study (in any case at least 5 times the half-life of the drug or a minimum of 14 days, whichever is longer), with the exception of paracetamol. Hormonal contraceptives and hormonal replacement therapy for women are allowed
5. 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
6. Blood donation: blood donations for 3 months before this study
7. Drug, alcohol, caffeine, tobacco: history of drug, alcohol (>1 drink/day for women and >2 drinks /day for men), caffeine (>5 cups coffee/tea/day) or tobacco abuse (10 cigarettes/day)
8. SARS-CoV-2 test: positive SARS-CoV-2 test on day -3 or -2
9. Virology: known positive test of Hepatitis B (HBs antigen), Hepatitis C (HCV antibodies), HIV 1 /2 (HIV Antigen/Antibodies combo)

10. Drug test: positive result at the drug test at screening
11. Alcohol test: positive alcohol breath test at screening or 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; vegans
13. Pregnancy (women only): positive or missing pregnancy test at screening or day -1; pregnant or lactating women.

Date of first enrolment
06/09/2021

Date of final enrolment
27/09/2021

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research S.A. - Phase I Unit
Via F. A. Giorgioli 14
Arzo
Switzerland
6864

Sponsor information

Organisation
Dompé farmaceutici S.p.A.

Funder(s)

Funder type
Industry

Funder Name
Dompé farmaceutici 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