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A study to assess the amount of active ingredient that reaches the blood circulation after administration in healthy men and women under fasting conditions of a new anxiolytic, sedative, and anticonvulsant mouth-dissolvable drug in comparison to the marketed tablets of Tavor®

Submission date
23/05/2024

Recruitment status
No longer recruiting

Registration date
24/05/2024

Overall study status
Completed

Last Edited
28/06/2024

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
A new orodispersible film containing lorazepam, an active ingredient commonly prescribed for a wide range of anxiety-related conditions, has been developed to provide an easy-to-take and rapidly dissolvable alternative to the marketed oral products for the short-term symptomatic treatment of anxiety and insomnia. This study is designed to investigate the amount of lorazepam that reaches the blood circulation after administration of the new lorazepam orodispersible film versus the reference product Tavor® 2.5 mg film-coated tablets, when administered to healthy men and women under fasting conditions, and evaluate if the two products produce similar levels of the active ingredient in the body after administration.

Who can participate?
Healthy men and women aged 18-55 years can participate. They must comprehend the full nature and purpose of the study, including possible risks and side effects, and cooperate with the investigator to comply with the requirements of the entire study.

What does the study involve?
The study will be conducted at the CROSS Research S.A. Phase I Unit Clinical Centre, in Arzo, Switzerland. Study participants will receive a single dose of IBSA Lorazepam 2.5 mg orodispersible film and a single dose of Tavor® 2.5 mg film-coated tablets in two study periods, according to a 2-way cross-over randomised design, with a wash-out interval of at least 7 days between the two administrations. Participants will have blood samples taken and vital parameters recorded at regular intervals.

What are the possible benefits and risks of participating?
Participating in this study will not bring any direct benefit to participants, except for the medical tests that will be performed during it. Lorazepam is a well-known active substance with established efficacy and tolerability. The formulation under investigation, IBSA Lorazepam 2.5 mg orodispersible film, has been already administered to men and women in a previous clinical study: the observed adverse events did not give any safety concern. Lorazepam 2.5 mg orodispersible formulations are already on the market and undesirable effects are known (above all, drowsiness, asthenia, depression, ataxia, confusion and muscle weakness). Overall, lorazepam administered as a single oral dose to healthy subjects is safe and well tolerated. However, as with all products, the appearance of allergic reactions or side effects that are known or not yet known cannot be ruled out.

Where is the study run from?
The study will be conducted at the CROSS Research S.A. Phase I Unit Clinical Centre, in Arzo, Switzerland.

When is the study starting and how long is it expected to run for?
September 2023 to March 2024

Who is funding the study?
IBSA Institut Biochimique S.A. (Switzerland)

Who is the main contact?
Dr. Milko Radicioni, clinic@croalliance.com

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Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
23CH-Lrz06

Study information

Scientific Title
Comparative bioavailability study of a new IBSA Lorazepam 2.5 mg orodispersible film and Tavor® (lorazepam) 2.5 mg film-coated tablets in healthy volunteers under fasting conditions

Acronym
IBSA Lorazepam 2.5 mg ODF pivotal BA

Study objectives
To compare the bioavailability of lorazepam after a single dose of IBSA Lorazepam 2.5 mg orodispersible film versus the reference product Tavor® 2.5 mg film-coated tablets, when administered to healthy men and women under fasting conditions.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 08/11/2023, Canton Ticino Ethics Committee (c/o Ufficio di Sanità, via Orico 5, Bellinzona, 6501, Switzerland; +41918143057; beatrice.giberti-gai@ti.ch), ref: 2023-01937 CE4476

Study design
Single centre single-dose open-label randomized 2-way cross-over pivotal bioavailability study

Primary study design

Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Pharmaceutical testing facility

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Lorazepam will be administered to healthy volunteers

Interventions
Each subject will receive a single oral dose of IBSA Lorazepam 2.5 mg orodispersible film and Tavor® 2.5 mg film-coated tablets under fasting conditions, in two study periods, with a wash-out interval of at least 7 days between the two administrations, according to a 2-way cross-over randomised design.
The investigational medicinal products will be orally administered on Day 1 of each study period at 08:00±1h as follows:
- one orodispersible film of IBSA Lorazepam 2.5 mg without water
- one film-coated tablet of Tavor® 2.5 mg with 150 mL of still mineral water
Just before the administration of IBSA Lorazepam 2.5 mg orodispersible film, the Investigator or deputy will take the orodispersible film out of the packaging. To avoid its inadvertent breakage, the Investigator or deputy shall:
1. take the envelope and hold it with the side not sealed facing up
2. gently peel both parts of the envelope and then hold each between his/her thumb and index fingers using one hand for each part
3. carefully tear both parts of the envelope in opposite directions until they will be separated. The film will be visible and placed on one of the separated envelope parts.
The Investigator or deputy will place the film directly on the subject's tongue. The Investigator will wear gloves during the administration procedure. The film will dissolve rapidly. Subjects will let the orodispersible film completely dissolve in their mouth. It must not be swallowed whole and must not be chewed or broken. The subject will be allowed to swallow saliva as the film dissolves in the mouth. In detail, once the subject feels that the film has completely dissolved, he /she will inform the Investigator who will inspect the subject’s mouth and verify the complete dissolution in the mouth. If the subject does not inform the Investigator within two minutes of the administration, his/her mouth will be checked by the Investigator at two and again at three minutes, if needed. If, upon inspection at two or three minutes, the film is already dissolved, the time of mouth check will be recorded as dissolution end time. If the film is not completely dissolved within 3 min, the subjects will be allowed to swallow without water. In this case, the dissolution end time will be considered as not applicable. The exact date and time of orodispersible film administration (defined as the time at which the film is placed on the subject’ s tongue by the Investigator or deputy) and the time of complete dissolution of the film (no residues present at inspection of the oral cavity by the Investigator or deputy) will be recorded. The occurrence of inadvertent chewing and/or breaking and/or swallowing will be recorded.

For administration of Tavor® 2.5 mg film-coated tablets, the subject will swallow the tablet with 150 mL of still mineral water. The tablet must be swallowed whole and must not be chewed or broken. The occurrence of inadvertent chewing and/or breaking will be recorded. Product administration date and time will be recorded as well.

Intervention Type
Drug

Pharmaceutical study type(s)
Bioequivalence

Phase
Phase I

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

Primary outcome measure
Rate (Cmax) and extent (AUC0-t) of lorazepam absorption in plasma measured from plasma samples taken at pre-dose (0) and at 0.5 (30 min), 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 16, 24, 36, 48 and 72 h post-dose after single dose administration of IBSA Lorazepam 2.5 mg orodispersible film and Tavor® 2.5 mg film-coated tablets under fasting conditions.

Secondary outcome measures
1. Time to peak (Tmax), relative bioavailability (Frel) and, if feasible, area under the concentration-time curve extrapolated to infinity (AUC0-inf), percentage of the residual area extrapolated to infinity in relation to the total AUC0-inf (%AUCextra), half-life (t1/2) and terminal elimination rate constant (λZ) of plasma lorazepam measured from plasma samples taken at pre-dose (0) and at 0.5 (30 min), 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 16, 24, 36, 48 and 72 h post-dose after single-dose administration of IBSA Lorazepam 2.5 mg orodispersible film and Tavor® 2.5 mg film-coated tablets under fasting conditions
2. All adverse events occurring after the informed consent signature but before the first dose of the investigational medicinal product (PTAEs), all adverse events occurring or worsening after the first dose of the investigational medicinal product (TEAEs), vital signs (blood pressure and heart rate, measured at the screening visit, on Day -1 of each study period, on Days 1-4 of each study period at pre-dose (0), 1.5, 3, 24, 48 and 72 h post-dose and at early termination visit [ETV] as applicable), body weight (measured at screening and final visit/ETV as applicable), physical examinations (performed at screening and final visit/ETV as applicable), clinical laboratory parameters (haematology, blood chemistry and urine analysis performed at screening and final visit/ETV as applicable; virology performed at screening; urine drug screening test and alcohol saliva test performed at screening and on Day -1 of each study period; a COVID-19 rapid test performed on Day -1 of each study period; serum pregnancy test performed at screening; urine pregnancy test on Day -1 of each study period), ECG (performed at screening and final visit/ETV as applicable).

Overall study start date
11/09/2023

Completion date
08/03/2024

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and Age: men and women, 18-55 years old inclusive
3. Body Mass Index: 18.5-30 kg/m2 inclusive
4. Vital signs: systolic blood pressure 100-139 mmHg, diastolic blood pressure 50-89 mmHg, heart rate 50-99 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 cooperate with the Investigator and to comply with the requirements of the entire 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. 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
6.2. A male sexual partner who agrees to use a male condom with spermicide
6.3. A sterile sexual partner
or:
True abstinence (i.e., refraining from heterosexual intercourse when this is in line with the preferred and usual lifestyle of the subject). Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), lactational amenorrhea, and withdrawal are not acceptable.
Women of non-child-bearing potential or in post-menopausal status for at least 1 year will be admitted. For all women, pregnancy test results must be negative at screening and Day -1.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
20

Total final enrolment
20

Key exclusion criteria
1. Electrocardiogram (12-lead ECG in supine position): clinically significant abnormalities
2. Physical findings: clinically significant abnormal physical findings which could interfere with

the objectives of the study; presence of mouth lesions or any other oral mucosa alteration; presence or history (within 28 days) of any tongue piercings; presence of any partials, braces or dentures
3. Laboratory analyses: clinically significant abnormal laboratory values indicative of physical illness
4. Allergy: ascertained or presumptive hypersensitivity to the active principle or formulations' ingredients or both; 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, skin, haematological, endocrine, immunological or neurological diseases that may 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 women will not be allowed
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 [>1 drink/day for women and >2 drinks/day for men, defined according to the USDA Dietary Guidelines 2020-2025], caffeine (>5 cups coffee/tea/day) or tobacco abuse (>=10 cigarettes/day)
10. SARS-CoV-2 test: positive Covid-19 rapid test at Day -1
11. Drug test: a positive result at the drug test at screening or Day -1
12. Alcohol test: positive alcohol saliva test at screening or Day -1
13. Diet: abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits in the 4 weeks before this study; vegetarians
14. Pregnancy (women only): positive or missing pregnancy test at screening or Day -1, pregnant or lactating women.

Date of first enrolment
29/01/2024

Date of final enrolment
31/01/2024

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research S.A.
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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
IBSA Institut Biochimique S.A.

Results and Publications

Publication and dissemination plan
To date, there are no plans to public the study results on scientific journals.

Intention to publish date
31/12/2024

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		27/06/2024	28/06/2024	No	No