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A comparative bioavailability study of ethinyl estradiol/etonogestrel vaginal ring in healthy female subjects

Submission date
17/09/2025

Recruitment status
No longer recruiting

Registration date
23/09/2025

Overall study status
Completed

Last Edited
23/09/2025

Condition category
Pregnancy and Childbirth

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
This study compares the bioavailability (how much of a medicine gets into your blood) and establishes bioequivalence of two different products of ethinylestradiol/etonogestrel vaginal ring. The aim is to compare how much of each product will be absorbed into the body, to see if they work in the same way.

Who can participate?
Healthy female volunteers aged 18 to 45 years.

What does the study involve?
This study was carried out at one location. Participants were randomly assigned to try two different products, one after the other, using a specific type of ring each time. The study was done in two parts, with the order of the products swapped for different groups. The test product contains etonogestrel/ethinylestradiol 8.25/2.6 mg in comparison to etonogestrel /ethinylestradiol 11.00/3.474 mg of the existing Ornibel® formulation and was compared with Nuvaring® (etonogestrel/ ethinylestradiol 11.7/2.7 mg) (reference product).

What are the possible benefits and risks of participating?
The benefits are the improvement in the implementation of a new drug system with a nominal reduction of 20% in the vaginal ring. This will lead to a general reduction in the exposure of hormones into the environment. The classical risks are all those associated with the use of hormonal combined contraceptives.

Where is the study run from?
Exeltis Germany GmbH

When is the study starting and how long is it expected to run for?
July 2023 to December 2023

Who is funding the study?
Laboratorios Liconsa, Spain

Who is the main contact?
Dr Pedro-Antonio Regidor, pedro-antonio.regidor@exeltis.com

Contact information

Type(s)
Public, Scientific, Principal Investigator

Contact name
Dr Pedro Antonio Regidor

ORCID ID
https://orcid.org/0000-0002-9551-2847

Contact details
Adalperostr. 84
Ismaning
Germany
85737
+49 01738938132
pedro-antonio.regidor@exeltis.com

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CEO-P6-532

Study information

Scientific Title
Single-dose crossover comparative bioavailability study of ethinyl estradiol/etonogestrel vaginal ring (delivering 0.015 mg/0.12 mg per day) worn for 28 days in healthy female subjects

Acronym
CEO-P6-532

Study objectives

The purpose of this study is to determine and compare the amount of study drug that gets into the blood after the insertion of one of the two vaginal ring formulations of ethinylestradiol /etonogestrel. Another objective of this study is to determine the safety and tolerability of both formulations as well as evaluate the user-friendliness of the vaginal rings. Lastly, this study will examine the local irritation and occurrence of bleeding/spotting in both formulations. The two formulations are manufactured by two different companies. Each formulation contains the same amount of drug. One of these two formulations (Reference) is currently being sold in Europe (and may differ from the product marketed in Canada). The other formulation (Test) is considered investigational, which means it is not approved by Health Canada for use outside of research studies like this one.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/07/2023, Advarra Canada (372 Hollandview, Suite 300, Aurora, L4G0A5, Canada; +1 905-707-7989; cirbi@advarra.com), ref: 2021-EEVR0508-PK-02 / CEO-P6-532

Study design
Single-dose crossover comparative bioavailability study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital, Laboratory, Medical and other records

Study type(s)
Treatment, Efficacy

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
Pharmacological data of two vaginal contraceptive rings

Interventions
Vaginal contraceptive ring containing: two female sex hormones – ethinylestradiol and etonogestrel. The ring slowly releases these hormones into the blood circulation. The ring releases ethinylestradiol and etonogestrel at an average amount of 0.015 mg and 0.12 mg, respectively, per 24 hours, over a period of 4 weeks.

General Procedure of the Study
This study will be conducted at one clinical site in two clinical periods. The removal of the first vaginal ring and the insertion of the second vaginal ring will be separated by at least 28 days. This procedure ensures that the study drug taken in the previous period is no longer detectable

in the blood at the beginning of the next period of the study. The first stay of each period (vaginal ring insertion) will last approximately 38 hours (about 1 1/2 days). The second stay of each period (vaginal ring removal will last approximately 24 hours (about 1 day). The total length of the study will be approximately 91 days, not including the screening period.

Each period corresponds to the insertion of one of the two vaginal ring formulations of ethinylestradiolethinyl estradiol/etonogestrel and its subsequent removal about 28 days (4 weeks) later. The formulation you will receive first will be random (by chance, like flipping a coin).

1st stay at the clinical site each period of the study:
• Patients will arrive at the clinical site at the time indicated by the clinical staff before vaginal ring insertion.
• They will stay at the clinical site until 24 hours after each vaginal ring insertion. However, for your safety, you will be asked to stay longer if the study doctor decides you may have important undesirable effects or health problems (side effects).
• They will return to the clinical site 15 more times after vaginal ring insertion (for 15 blood draws). You must arrive at the clinical site at least 20 minutes before the scheduled sampling times.

2nd stay at the clinical site each period of the study:
• Patients will arrive at the clinical site at the time indicated by the clinical staff before vaginal ring removal.
• They will stay at the clinical site until 24 hours after each vaginal ring removal. However, for your safety, you will be asked to stay longer if the study doctor decides you may have important undesirable effects or health problems (side effects).
• They will return to the clinical site 3 more times after vaginal ring removal (for 3 blood draws). You must arrive at the clinical site at least 20 minutes before the scheduled sampling times.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Bioequivalence

Phase
Phase I

Drug/device/biological/vaccine name(s)
Test vaginal contraceptive ring containing etonogestrel/ethinylestradiol 8.25/2.6 mg, reference Nuvaring® vaginal contraceptive ring containing etonogestrel/ethinylestradiol 11.7/2.7 mg

Primary outcome measure
Serum etonogestrel/ethinylestradiol (3-Ketodesogestrel and ethylestradiol) levels were measured using high-performance liquid chromatography technology with tandem mass spectrometry detection. Blood samples were taken before and at 1.00, 3.00, 6.00, 9.00, and 12.00 hours to perform PK measures. The next hours were 24, 48, 72, 96, 120, 168, 216, 264, 312, 336, 360, 432, 504, 528, 576, and 624, 672, 675, 678, 684, 688, 696, 720, 744, and 792 hours after vaginal ring insertion (for Etonogestrel alone).

Secondary outcome measures

1. Safety and tolerability measured using data collected from electronic Case Report Forms (eCRF) at the end of the study
2. User-friendliness measured using an electronic diary at the end of period 1 (after 28 days) and period 2 (after 28 days)

Overall study start date
05/07/2023

Completion date
01/12/2023

Eligibility

Key inclusion criteria
1. Signature and dating of this consent form
2. Review of medical and medication history
3. Recording of demographical data (age, sex, race, body weight, height, and BMI) and alcohol and smoking habits
4. Full physical exam
5. Vital signs measurement (blood pressure, heart rate and body temperature)
6. Electrocardiogram (ECG) - a recording of the electrical activity of your heart
7. Blood and urine samples for laboratory tests
8. Blood pregnancy test
9. Alcohol breath test
10. Urine drug screen to test for drugs of abuse (amphetamines, barbiturates, cannabinoids, cocaine, cotinine, opiates and phencyclidine)
11. Urine cotinine test to find out if you have smoked nicotine products
12. Breast and Gynecological exam
13. Pap smear to detect vaginal or uterine cancer (if not performed at Altasciences in the past 12 months)
14. Blood test for HIV and hepatitis B and C. Note that a positive test result must be reported to the public health authorities, as required by law

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Target number of participants

40

Total final enrolment
40

Key exclusion criteria
1. BMI >=30 kg/m2
2. No clinically significant pathological physical examination or laboratory results (haematology, general biochemistry, ECG, urinalysis, and PAP smear) or medical history

Date of first enrolment
01/08/2023

Date of final enrolment
01/12/2023

Locations

Countries of recruitment
Canada

Study participating centre
Altasciences
1200 Beaumont Ave
Mount-Royal
Canada
H3P3P1

Sponsor information

Organisation
Laboratorios Liconsa

Sponsor details
Avenida Miralcampo 7
Azuqueca de Henares
Spain
19200
+34620825788
jorge.aviles@chemogroup.com

Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Laboratorios Liconsa

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
01/10/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Pedro-Antonio Regidor, pedro-antonio.regidor@exeltis.com

IPD sharing plan summary
Available on request