A randomized, open label balanced two period, two-treatment, two-sequence crossover study to evaluate the effect of food on the pharmacokinetics of buspirone after a single oral administration of Lybridos in healthy female subjects

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Primary objective1. To determine the effect of food on the pharmacokinetics of buspirone administered as the Lybridos formulationSecondary objective1. To evaluate the safety and tolerability of a single dose of Lybridos under fasted and fed...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Sexual dysfunctions, disturbances and gender identity disorders
Study type	Interventional

Summary

ID

NL-OMON41098

Source
ToetsingOnline

Brief title
Lybridos Food Effect

Condition

- Sexual dysfunctions, disturbances and gender identity disorders

Synonym
problems with sexual functioning, Sexual dysfunction

Research involving
Human

Sponsors and support

Primary sponsor: EB FlevoResearch BV
Source(s) of monetary or material Support: EB FSD BV

Intervention

Keyword: Buspiron, Female Sexual Dysfunction, Lybridos, Randomized

Outcome measures

Primary outcome

Pharmacokinetic

90% CI ratio for both AUC0-inf and Cmax

Secondary outcome

Pharmacokinetic

Difference in Tmax and tlag

and

- Area under the concentration time curve (AUC)

- Peak exposure (Cmax)

- Time to peak exposure (Tmax)

- Lag time (tlag)

- Terminal elimination half-life (t*)

Safety

A. Nature, frequency and severity of AEs

B. Vital signs and 12-lead ECG

C. Safety laboratory tests (urinalysis, haematology, biochemistry)

Study description

Background summary

Sexual dysfunction
In many mammalian species, female sex steroids are necessary for the expression of female sexual behaviour. In most animals, copulation is limited to the period of ovulation. Humans (as well as higher primates), however, show sexual intercourse also outside the periovulatory period. Testosterone is involved in female sexual behaviour. A complete loss, decreased libido, or absence of desire for sexual activity is common after bilateral oophorectomy, adrenalectomy, and after natural menopause, while substitution with testosterone has been shown to improve sexual motivation and performance.

The 3 (transitional and overlapping) phases of the human sexual response can each be disrupted, leading to low sexual desire, sexual arousal problems, and hampered orgasm. The phases are regulated by relatively independent neurotransmitter functions, and dysfunctions may be amenable to psychopharmacological treatment. Traditionally, motivated behaviours have been divided into appetitive and consummatory components. Activities aimed at obtaining reward and satisfactions belong to the appetitive component. The fundamental appetitive motivational process is an intrinsic brain function and is especially related to the predictive value of stimuli for reward.
Processing of motivationally relevant information (i.e., stimuli predicting reward) causes an increase in activity of the meso-accumbens dopaminergic system (i.e., dopamine neurons of the ventral tegmental area [VTA] innervating the nucleus accumbens). The activity of this system is increased during flexible approach behaviour when anticipating reward related to copulation.
Increasing activity in these dopaminergic pathways facilitates sexual motivation, in particular anticipatory sexual behaviour.

Anticipating sexual reward will produce arousal of the genitals, in which at least 2 key neurotransmitters are involved: acetylcholine and nitric oxide (NO). Acetylcholine and NO both promote erections in men and lubrication and swelling in women. Orgasm, the consummatory phase of human sexual response, is facilitated by descending spinal noradrenergic fibres and innervation of the genitals, and inhibited by descending spinal serotonergic fibres.

Study objective

Primary objective
1. To determine the effect of food on the pharmacokinetics of buspirone

administered as the Lybridos formulation

Secondary objective
1. To evaluate the safety and tolerability of a single dose of Lybridos under fasted and fed conditions

Study design

This will be a randomized, open-label balanced two-period, two-treatment, two-sequence crossover study in healthy female subjects to evaluate the effect of food on the pharmacokinetics (PK) of buspirone after a single dose of Lybridos. In addition, safety and tolerability of Lybridos administered after fed and fasted conditions will be evaluated.

All subjects will complete a screening visit. Prior to the day of dosing, eligible subjects will stay overnight (O/N) (at least 10 hours) in an environment controlled for fasting conditions. An intravenous cannula will be placed in a vein in each subject prior to dosing (if possible) to provide access for regular blood sampling.

Randomization will ensure that each subject will receive each of the following treatments (A and B) on two separate occasions, being:
A. Fed + Lybridos
B. Fasted + Lybridos
And is assigned to one of the following treatment sequences: A-B or B-A.

On the day of dosing, subjects in treatment A will take a high fat, high calorie meal (50% of the caloric intake of 800-1000 kcal) on site. Lybridos is administered 30 minutes after the start of the food intake and the meal should be completed within this 30 minutes time frame. No intake of water is allowed the hour prior to and 1 hour post administration of the drug. Lybridos will be taken with 240 mL water and subject will abstain from food intake the following 4 hours. The food intake will be standardized for all patients during 12 hours post dose.

For subjects in treatment B, administration of Lybridos is taken with 240 mL water. No intake of water is allowed the hour prior to and 1 hour post administration of the drug. Next 4 hours, the subject will abstain from food intake. The food intake will be standardized for all patients during 12 hours post dose.

Both periods will be separated by a washout period of at least 1 week between the dosing of the 1st period and dosing of the 2nd period.

Intervention

NA

Study burden and risks

NA

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Provision of written informed consent
2. Females between 18 and 55 years of age (both inclusive)
3. Healthy based on medical history, physical examination, electrocardiogram, laboratory values and vital signs

4. Body mass index (BMI) >=18 kg/m2 and <= 30 kg/m2
5. Venous access sufficient to allow blood sampling as per protocol;

Exclusion criteria

1. Systolic blood pressure >= 140 mmHg and/or diastolic blood pressure >= 90 mmHg
2. Systolic blood pressure < 90 mmHg and/or diastolic blood pressure< 50 mmHg
3. Use of oral contraceptive containing anti-androgens (e.g. cyproteron) or anti(androgenic) progestogens (drospirone, dienogest, chlormadinone acetate and norgestrel)
4. Use of any or hormone replacement therapy (HRT) containing more than 50 µg/day of estrogen
5. Pregnancy (note: an urine pregnancy test will be performed in all women prior to the administration of study medication)
6. Lactating or delivery in the previous 6 months
7. Perimenopausal status (cycle shortening/irregular menstrual bleeding in the last 12 consecutive months and/or occurrence of vasomotor symptoms (e.g. hot flashes, night contraceptive sweating) in combination with elevated FSH levels (>40 IU/L) for women from age 40 onwards; in women with a history of hysterectomy, perimenopausality can be assessed by FSH levels (> 40 IU/L) and/or vasomotor symptoms)
8. Use of any drugs from two weeks prior to admission to the research unit until the follow-up visit, except for allowed oral contraceptives and pain relief (e.g. paracetamol up to 1.5 g per day)
9. Known or suspected hypersensitivity to any of the components of the formulation
10. Liver function tests (i.e., ALT, AST and bilirubin) significantly above the upper limit of normal at repeated measures
11. Any clinically significant history of any other disease or disorder - gastrointestinal, cardiovascular, respiratory, renal, hepatic, neurological, dermatological, psychiatric or metabolic as judged by the medical investigator
12. Smoking
13. Unwilling or unable to refrain from consuming grapefruit juice, star fruit, and St. Johns Wort 24 hours before and after intake of medication
14. Current regular use of any illicit drugs or history of excessive drinking within 3 months prior to admission to the research unit and/or unwilling or unable to refrain from products containing alcohol from 24 hours before admission and during the stay in the research unit
15. Donation of blood within 3 months prior to admission to the research unit
16. Positive serology test for HBsAg, anti HAV (IgM), anti HCV or anti HIV 1+2
17. Subjects who, in the opinion of the investigator, are not likely to complete the trial for any reason
18. Participation in any clinical study within 1 month prior to the expected date of enrolment into the study.
19. Employees of the sponsor or CRO involved in the study

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-03-2015
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Buspar
Generic name:	Buspirone
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Testosterone
Generic name:	Testosterone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	23-10-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	18-11-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 22366
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-003318-99-NL
CCMO	NL50357.056.14
OMON	NL-OMON22366