An outpatient phase 3 efficacy study of Ecopipam (PSYRX 101) in the symptomatic treatment of self-injurious behavior in subjects with Lesch-Nyhan disease.

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON37257

Source
ToetsingOnline

Brief title
N/A

Condition

- Other condition
- Chromosomal abnormalities, gene alterations and gene variants
- Movement disorders (incl parkinsonism)

Synonym
HPRT gene mutation, Lesch-Nyhan disease

Health condition

zelfverwondend gedrag

Research involving
Human

Sponsors and support

Primary sponsor: Psyadon Pharmaceuticals Inc.
Source(s) of monetary or material Support: farmaceutisch bedrijf

Intervention

Keyword: behavior problems inventory, Ecopipam, Lesch-Nyhan disease, self-injurious behavior

Outcome measures

Primary outcome

The primary endpoint is the Behavior Problems Inventory (self-injurious

behavior subscales for severity and frequency) as assessed by the caregiver.

Secondary outcome

Secondary parameters that will be analyzed are the total and other subscales

of the Behavior Problems Inventory, and the withdrawal and maintenance effects

of Ecopipam. Safety data that will be evaluated include adverse events,

clinical laboratory results, vital signs, and other results.

Study description

Background summary

Ecopipam is an investigational drug, it has not yet been granted marketing approval by regulatory agencies such as the European Medicines Agency (EMA). Ecopipam is being investigated for use in the symptomatic treatment of self-injurious behavior in subjects with Lesch-Nyhan Disease (LND).

LND is a very rare neurogenetic disorder caused by a mutation of the HPRT gene. It is characterized by uric acid accumulation, intellectual impairment,

movement disorders and self-injurious behavior. Estimates reveal an incidence of LND of 1 in 235,000 live births and a prevalence of 1 case per million.

D1-receptor super-sensitivity may be a mechanism for the repetitive and compulsive self-injurious behaviors. Ecopipam is a selective antagonist of the D1-receptor family. This study aims to assess the efficacy and safety of Ecopipam in the symptomatic relief of self-injurious behavior in subjects with LND.

Study objective

The primary objective of this study is to assess the efficacy of Ecopipam to reduce self-injurious behaviors (SIB) in adults and children with Lesch-Nyhan Disease (LND) in an outpatient setting. The secondary objectives of this study are to assess the effect of withdrawal, maintenance, and safety of Ecopipam in subjects with LND.

Study design

Protocol PSY102 is a multicenter, randomized, double-blind, 3-period crossover study, with an open-label extension. In an outpatient setting, subjects will be randomized to receive placebo or Ecopipam as the initial treatment. Double-blind treatment will occur over a 19 to 20 week period with subjets receiving 1 of the following 2 sequences: Sequence A - placebo, Ecopipam, placebo or Sequence B - Ecopipam, Placebo, Ecopipam.

Ecopipam (50 or 100 mg, depending on weight) or matching placebo will be taken daily at bedtime. Subjects who tolerate double-blind treatment will be allowed to enter the open-label extension and will receive Ecopipam (50 or 100 mg, depending on weight) for up to 52 weeks, which will be taken daily at bedtime.

Intervention

* Double-blind phase
Subjects will receive Ecopipam (50 or 100 mg, based on body weight) or matching placebo daily at bedtime. No study drug will be administered during the follow-up period (between treatment period 3 and the start of the open-label phase).

* Open-label extension phase
Subjects will receive a single daily dose of Ecopipam (50 or 100 mg, based on body weight) at bedtime.

Study burden and risks

Currently, there are no medications approved for the treatment of

self-injurious behavior in patients with Lesch-Nyhan Disease. The study aims to assess the efficacy and safety of Ecopipam in the symptomatic relief of self-injurious behavior in subjects with Lesch-Nyhan Disease. Ecopipam has been studied in over 2 thousand human subjects in clinical studies and showed to be well tolerated. In a study with Ecopipam in subjects with Lesch-Nyhan Disease, the most common side-effects were: sleepiness, upset stomach and involuntary muscle movement (dystonia).

The total study duration for a subject will be approximately 17 months (up to 18 weeks double-blind treatment, 1 to 2 week follow-up, followed by up to 52 weeks on open-label extension). At most, 3 clinic visits and 6 home visits will be performed. Additionally, the caregiver will be contacted every 4 weeks by telephone during the open-label extension.

During the trial following assessments will be performed (see schedule of procedures/assessments on page 31 of the protocol):
- Physical examination: 1x
- Vital signs (systolic and diastolic blood pressure, radial pulse, respiration, body temperature and weight): 9x
- Measurement of height: 1x
- Blood drawing: 3x (total approx. 30 ml)
- Urine sample: 3x
- Pregnancy test (urine): 3x (females of childbearing potential only).

The Behavior Problems Inventory (22x) and Caregiver Global Impression (6x) will be completed by the caregiver.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

* Subjects must have classic LND as defined by (a) characteristic clinical syndrome (evidence of overproduction of uric acid, severe generalized dystonia, frequent and persistent SIB, and cognitive impairment) and (b) laboratory confirmation for mutation of the HPRT gene or severe deficiency of the associated enzyme.
* Subjects must have a minimum combined score of 20 on the Behavior Problems Inventory (BPI) SIB subscales for frequency and severity as assessed by the caregiver.
* Subjects must have a minimum score of 4 on the Physician*s Global Impression (PGI) severity scale.
* Subject must be >= 6 years old.
* Subjects must weigh > 10 kg.

Exclusion criteria

* Subjects who are currently treated with medications for seizures.
* Subjects who are on neuroleptics or dopamine-depleting agents.
* Subjects with impaired renal function as defined by a serum creatinine >1.5 mg/dL.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-11-2012
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	Ecopipam

Ethics review

Approved WMO Date:	26-10-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-01-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-03-2013
Application type:	First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-002662-12-NL
CCMO	NL41689.091.12
Other	Wordt later geregistreerd