



## Clinical trial results: Interventional, Open-label, Flexible-dose Extension Study of Brexpiprazole in Patients With Schizophrenia Summary

EudraCT number	2012-002705-21
Trial protocol	CZ EE SK PL RO
Global end of trial date	30 December 2015

### Results information

Result version number	v1 (current)
This version publication date	14 January 2017
First version publication date	14 January 2017

### Trial information

#### Trial identification

Sponsor protocol code	14644B
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01810783
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	LundbeckClinicalTrials@lundbeck.com , H. Lundbeck A/S, LundbeckClinicalTrials@lundbeck.com
Scientific contact	LundbeckClinicalTrials@lundbeck.com , H. Lundbeck A/S, LundbeckClinicalTrials@lundbeck.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 December 2015
Global end of trial reached?	Yes
Global end of trial date	30 December 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To determine the safety and efficacy of brexpiprazole during long-term treatment

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2008) and ICH Good Clinical Practice (1996)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 July 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 50
Country: Number of subjects enrolled	Estonia: 6
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Russian Federation: 52
Country: Number of subjects enrolled	Serbia: 19
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Ukraine: 64
Worldwide total number of subjects	210
EEA total number of subjects	25

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	209
From 65 to 84 years	1
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects who met each of the inclusion and none of the exclusion criteria were eligible to participate in the study

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	Brexpiprazole
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Brexpiprazole
Investigational medicinal product code	
Other name	Rexulti
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Brexpiprazole: 1 to 4 mg/day, once daily, tablets, orally. The patients received 2 mg/day brexpiprazole on Day 1. If a patient could not tolerate the 2 mg dose on Day 1, the dose was decreased to 1 mg/day at Day 2. The patients received 1 or 2 mg/day from Days 2 to 7, 1, 2, or 3 mg/day from Days 8 to 14, and 1, 2, 3, or 4 mg/day from Day 15 to completion of the Treatment Period (up-titration).

Number of subjects in period 1	Brexpiprazole
Started	210
Completed	101
Not completed	109
Consent withdrawn by subject	22
Adverse event, non-fatal	32
Administrative or other reasons(s)	23
Lost to follow-up	10
Non-compliance with IMP	4
Lack of efficacy	12
Protocol deviation	5
Not treated	1



## Baseline characteristics

### Reporting groups

Reporting group title	Overall Study
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Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	210	210	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	209	209	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	40.89		
standard deviation	± 11.35	-	
Gender categorical			
Units: Subjects			
Female	113	113	
Male	97	97	
Race			
Units: Subjects			
White	173	173	
Black or African American	35	35	
Other	1	1	
Native Hawaiian Or Other	1	1	

## End points

### End points reporting groups

Reporting group title	Brexpiprazole
Reporting group description: -	

### Primary: Safety and tolerability

End point title	Safety and tolerability <sup>[1]</sup>
End point description:	
Number of treatment emergent adverse events (TEAEs)	
End point type	Primary

End point timeframe:

Up to 52 weeks and a safety follow-up by telephone contact or clinic visit after 30 days after the last dose of investigational medicinal product (IMP)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No comparison between parameters were done

<b>End point values</b>	Brexpiprazole			
Subject group type	Reporting group			
Number of subjects analysed	209			
Units: Number	337			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

First dose to follow-up

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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### Reporting groups

Reporting group title	Brex
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Reporting group description:

Brex

Serious adverse events	Brex		
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 209 (14.83%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung carcinoma cell type unspecified stage iv			

subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Grand mal convulsion			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed <sup>[1]</sup>	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Social stay hospitalisation			
subjects affected / exposed	2 / 209 (0.96%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Panic attack			

subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			
subjects affected / exposed	2 / 209 (0.96%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Schizophrenia			
subjects affected / exposed	18 / 209 (8.61%)		
occurrences causally related to treatment / all	6 / 18		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	2 / 209 (0.96%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Peritonsillar abscess			
subjects affected / exposed	1 / 209 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Gender specific adverse event

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Brex		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 209 (22.49%)		
Investigations			
Weight increased			
subjects affected / exposed	22 / 209 (10.53%)		
occurrences (all)	23		
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 209 (8.61%)		
occurrences (all)	21		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	17 / 209 (8.13%)		
occurrences (all)	21		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported