

**Clinical trial results:  
Pregabalin for anxiety comorbidity in patients with schizophrenia  
(PACS)****- A Double-blinded Randomized Placebo Controlled Trial****Summary**

EudraCT number	2010-024488-42
Trial protocol	DK
Global end of trial date	15 August 2016

**Results information**

Result version number	v1 (current)
This version publication date	30 September 2021
First version publication date	30 September 2021

**Trial information****Trial identification**

Sponsor protocol code	2010-024488-42-PACS
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01496690
WHO universal trial number (UTN)	-
Other trial identifiers	The North Dk Region Comm. on Health Res. Ethics: N20100097

Notes:

**Sponsors**

Sponsor organisation name	Aalborg Psychiatric Hospital
Sponsor organisation address	Mølleparkvej 10, Aalborg, Denmark, 9000
Public contact	Centre for Psychosis Research, Aalborg University Hospital, Aalborg Psychiatric Hospital, 0045 29323543, ole.schjerner@rsyd.dk
Scientific contact	Centre for Psychosis Research, Aalborg University Hospital, Aalborg Psychiatric Hospital, 0045 29323543, ole.schjerner@rsyd.dk

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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	01 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 August 2016
Global end of trial reached?	Yes
Global end of trial date	15 August 2016
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

To investigate the effect and tolerability of pregabalin for schizophrenic patients that suffer from comorbid anxiety.

Protection of trial subjects:

All participants provided written informed consent to participation. This study was performed in accordance with the ICH-CGP guidelines and the Declaration of Helsinki. The Local Ethics Committee, the Danish Health Authority and the Danish Data Protection Agency approved the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Denmark: 54
Worldwide total number of subjects	54
EEA total number of subjects	54

Notes:

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**Subjects enrolled per age group**

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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)	54
From 65 to 84 years	0



## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited from all five regions of Denmark. First patient was included at 5th of March 2012 and last patient ended the study at 15th of August 2016. The study was ended before sample size goal was met due to failure in accessing eligible patients.

### Pre-assignment

Screening details:

Patients aged 18 to 65 years with a diagnosis of schizophrenia (ICD-10: F20.0 to F20.3 or F20.9). No changes in primary psychopharmacologic treatment (antipsychotics, antidepressants and sedatives) for at least 4 weeks. Severity of anxiety was measured using the Hamilton Anxiety Scale. Patients with a total score above 15 were included.

### Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Randomization was done in blocks with variable block size (4, 6 and 8) to maintain an equal allocation of patients over time. Randomization sequence was generated by the Hospital Pharmacy, Aalborg University Hospital, Aalborg, Denmark. All research staff and patients were blinded to treatment allocation. Pregabalin capsules and placebo capsules were identical and provided by Pfizer Denmark.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Pregabalin

Arm description:

Active treatment

Arm type	Active comparator
Investigational medicinal product name	Pregabalin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pregabalin/placebo was initiated at 75 mg/d. After one week, dosage was increased to 150 mg/d and a flexible dosage regimen allowing weekly increments by 150 mg/d, up to a maximum of 600 mg/d — depending on effect and tolerability. Dosages  $\geq 450$  mg/d were divided in two doses. Compliance was calculated after 4 and 8 weeks.

<b>Arm title</b>	Placebo
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Arm description:

Placebo

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pregabalin/placebo was initiated at 75 mg/d. After one week, dosage was increased to 150 mg/d and a flexible dosage regiment allowing weekly increments by 150 mg/d, up to a maximum of 600 mg/d – depending on effect and tolerability. Dosages  $\geq 450$  mg/d were divided in two doses. Compliance was calculated after 4 and 8 weeks.

<b>Number of subjects in period 1</b>	Pregabalin	Placebo
Started	28	26
Completed	22	22
Not completed	6	4
Consent withdrawn by subject	-	1
Adverse event, non-fatal	3	2
Compliance below 70%	3	-
Protocol deviation	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Pregabalin
Reporting group description:	
Active treatment	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Reporting group values	Pregabalin	Placebo	Total
Number of subjects	28	26	54
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	26	54
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	11	7	18
Male	17	19	36

### Subject analysis sets

Subject analysis set title	End trial analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Difference between ratings at baseline and after 8 weeks of treatment on the Hamilton Anxiety Scale.	

Reporting group values	End trial analysis		
Number of subjects	54		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			

From 65-84 years 85 years and over			
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Gender categorical Units: Subjects			
Female	18		
Male	36		

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## End points

### End points reporting groups

Reporting group title	Pregabalin
Reporting group description:	
Active treatment	
Reporting group title	Placebo
Reporting group description:	
Placebo	
Subject analysis set title	End trial analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Difference between ratings at baseline and after 8 weeks of treatment on the Hamilton Anxiety Scale.	

### Primary: HAM-A14

End point title	HAM-A14
End point description:	
End point type	Primary
End point timeframe:	
8 weeks treatment	

End point values	Pregabalin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	26		
Units: HAM-A14 scale units	28	26		

### Statistical analyses

Statistical analysis title	Change in HAM-A14 score
Statistical analysis description:	
Difference between HAM-A14 ratings at baseline and after 8 weeks of treatment.	
Comparison groups	Pregabalin v Placebo
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	equivalence
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	5.9

Variability estimate	Standard deviation
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## Secondary: HAM-A6

End point title	HAM-A6
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End point description:

End point type	Secondary
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End point timeframe:

After 8 weeks treatment

End point values	Pregabalin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	26		
Units: HAM-A6 score	28	26		

## Statistical analyses

<b>Statistical analysis title</b>	Change in HAM-A6 scores
Comparison groups	Pregabalin v Placebo
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	equivalence
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	4
Variability estimate	Standard deviation

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

8 weeks of treatment

Assessment type	Systematic
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### Dictionary used

Dictionary name	None
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Dictionary version	0
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### Reporting groups

Reporting group title	Pregabalin
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Reporting group description:

Pregabalin/placebo was initiated at 75 mg/d. After one week, dosage was increased to 150 mg/d and a flexible dosage regiment allowing weekly increments by 150 mg/d, up to a maximum of 600 mg/d – depending on effect and tolerability. Dosages  $\geq$ 450 mg/d were divided in two doses. Compliance was calculated after 4 and 8 weeks.

Reporting group title	Placebo
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Reporting group description:

Pregabalin/placebo was initiated at 75 mg/d. After one week, dosage was increased to 150 mg/d and a flexible dosage regiment allowing weekly increments by 150 mg/d, up to a maximum of 600 mg/d – depending on effect and tolerability. Dosages  $\geq$ 450 mg/d were divided in two doses. Compliance was calculated after 4 and 8 weeks.

<b>Serious adverse events</b>	Pregabalin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 28 (10.71%)	1 / 26 (3.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Worsening of hallucinations			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt	Additional description: Suicide attempt using overdose of benzodiazepines		
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Pregabalin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 28 (100.00%)	26 / 26 (100.00%)	
Cardiac disorders			
Palpitations			
subjects affected / exposed	5 / 28 (17.86%)	4 / 26 (15.38%)	
occurrences (all)	5	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	11 / 28 (39.29%)	5 / 26 (19.23%)	
occurrences (all)	11	5	
Increased fatiguability			
subjects affected / exposed	9 / 28 (32.14%)	6 / 26 (23.08%)	
occurrences (all)	9	6	
Sedation			
subjects affected / exposed	5 / 28 (17.86%)	4 / 26 (15.38%)	
occurrences (all)	5	4	
Dystonia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Rigidity			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Hypokinesia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Hyperkinesia			
subjects affected / exposed	5 / 28 (17.86%)	1 / 26 (3.85%)	
occurrences (all)	5	1	
Tremor			
subjects affected / exposed	3 / 28 (10.71%)	3 / 26 (11.54%)	
occurrences (all)	3	3	
Akathisia			
subjects affected / exposed	7 / 28 (25.00%)	3 / 26 (11.54%)	
occurrences (all)	7	3	
Epileptic seizures			

subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	0 / 26 (0.00%) 0	
Paresthesia subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 3	2 / 26 (7.69%) 2	
Dizziness postural subjects affected / exposed occurrences (all)	6 / 28 (21.43%) 6	7 / 26 (26.92%) 7	
Headache subjects affected / exposed occurrences (all)	6 / 28 (21.43%) 6	6 / 26 (23.08%) 6	
Eye disorders Accommodation disorder subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 5	1 / 26 (3.85%) 1	
Gastrointestinal disorders Increased salivation subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 5	2 / 26 (7.69%) 2	
Dryness of mouth subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 4	5 / 26 (19.23%) 5	
Nausea subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 5	6 / 26 (23.08%) 6	
Diarrhoea subjects affected / exposed occurrences (all)	6 / 28 (21.43%) 6	4 / 26 (15.38%) 4	
Constipation subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 3	3 / 26 (11.54%) 3	
Reproductive system and breast disorders Increased sexual desire subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	0 / 26 (0.00%) 0	
Diminished sexual desire			

subjects affected / exposed occurrences (all)	6 / 28 (21.43%) 6	2 / 26 (7.69%) 2	
Orgasmic dysfunction subjects affected / exposed occurrences (all)	7 / 28 (25.00%) 7	3 / 26 (11.54%) 3	
<b>Skin and subcutaneous tissue disorders</b>			
Increased tendency to sweating subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	1 / 26 (3.85%) 1	
Rash subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 3	1 / 26 (3.85%) 1	
Pruritus subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	1 / 26 (3.85%) 1	
Photosensitivity reaction subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 3	0 / 26 (0.00%) 0	
Increased pigmentation subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 4	0 / 26 (0.00%) 0	
<b>Psychiatric disorders</b>			
Concentration difficulties subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 4	3 / 26 (11.54%) 3	
Failing memory subjects affected / exposed occurrences (all)	6 / 28 (21.43%) 6	5 / 26 (19.23%) 5	
Depression subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 5	9 / 26 (34.62%) 9	
Tension subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 4	4 / 26 (15.38%) 4	
Increased duration of sleep			

subjects affected / exposed occurrences (all)	15 / 28 (53.57%) 15	2 / 26 (7.69%) 2	
Reduced duration of sleep subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	3 / 26 (11.54%) 3	
Increased dream activity subjects affected / exposed occurrences (all)	6 / 28 (21.43%) 6	3 / 26 (11.54%) 3	
Emotional indifference subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 4	2 / 26 (7.69%) 2	
<b>Renal and urinary disorders</b>			
Micturition disorder subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 5	4 / 26 (15.38%) 4	
Polyuria subjects affected / exposed occurrences (all)	9 / 28 (32.14%) 9	2 / 26 (7.69%) 2	
<b>Metabolism and nutrition disorders</b>			
Weight gain poor subjects affected / exposed occurrences (all)	24 / 28 (85.71%) 24	9 / 26 (34.62%) 9	
Weight loss subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 3	7 / 26 (26.92%) 7	

## **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

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### **Online references**

<http://www.ncbi.nlm.nih.gov/pubmed/28919128>