Clinical trial results:
A Phase 3 double-blind, randomized, placebo-controlled, safety and efficacy study of once daily controlled release pregabalin in the treatment of patients with postherpetic neuralgia.

Summary

EudraCT number	2009-016766-86
Trial protocol	CZ SE SK BG DE HU DK PL HR
Global end of trial date	03 September 2014

Results information

Result version number	v1 (current)
This version publication date	06 March 2016
First version publication date	06 March 2016

Trial information

Trial identification

Sponsor protocol code	A0081224

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01270828
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc
Sponsor organisation address	235 E 42nd St,, New York,, United States,
Public contact	Clinical Trials.gov Call Center, Pfizer Inc.,, Pfizer, Inc., 011 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Clinical Trials.gov Call Center, Pfizer Inc.,, Pfizer, Inc., ClinicalTrials.gov_Inquiries@pfizer.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	02 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 September 2014
Global end of trial reached?	Yes
Global end of trial date	03 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of pregabalin CR compared with placebo in the durability of effect for the treatment of pain associated with PHN among patients who initially respond to single blind pregabalin. The secondary objectives were to evaluate the efficacy of pregabalin CR compared with placebo to relieve pain and to improve global assessment, functional status, and sleep; to assess treatment satisfaction with pregabalin CR compared with placebo; and to assess the safety and tolerability of the pregabalin CR formulation.

Protection of trial subjects:

The study was conducted in accordance with legal and regulatory requirements, as well as the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002), Guidance for Good Clinical Practice (International Conference on Harmonization [ICH] 1996), and the Declaration of Helsinki (World Medical Association 2008). In addition, the study was conducted in accordance with the protocol, the ICH Guideline on Good Clinical Practice (GCP), and applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 April 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Colombia: 8
Country: Number of subjects enrolled	Bulgaria: 41
Country: Number of subjects enrolled	Croatia: 7
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	India: 16
Country: Number of subjects enrolled	Poland: 21
Country: Number of subjects enrolled	Russian Federation: 91
Country: Number of subjects enrolled	Serbia: 6
Country: Number of subjects enrolled	Slovakia: 14
Country: Number of subjects enrolled	South Africa: 74
Country: Number of subjects enrolled	Sweden: 35
Country: Number of subjects enrolled	Taiwan: 6

Country: Number of subjects enrolled	Ukraine: 91
Country: Number of subjects enrolled	United States: 382
Worldwide total number of subjects	806
EEA total number of subjects	128

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)	382
From 65 to 84 years	402
85 years and over	22

Subject disposition

Recruitment

Recruitment details:

A total of 129 centers in 17 countries screened participants for the study, including 68 in the US, 6 in Bulgaria, 6 in Poland, 6 in Russia, 6 in the Ukraine, 5 in India, 5 in South Africa, 5 in Sweden, 4 in Slovakia, 3 in Colombia, 3 in Croatia, 3 in Germany, 2 in Denmark, 2 in Hong Kong, 2 in Serbia, 2 in Taiwan, and 1 in the Czech Republic.

Pre-assignment

Screening details:

The study consisted of 4 phases: Baseline (1 week [wk]): to determine study entry criteria; Single Blind (SB) (6 wks): to determine optimized dose; Double Blind (DB) (13 wks): responders with at least 50% improvement in pain at SB were considered and randomized to pregabalin or matching placebo; and DB taper phase (1 wk).

Period 1

Period 1 title	Pregabalin CR SB (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Arm title	Pregabalin CR SB

Arm description:

SB The participants with normal CLcr (≥60 mL/min) were treated with pregabalin 165 mg/day CR; those with low CLcr (>30 - <60 mL/min) received 82.5 mg/day pregabalin CR. Subsequently, the pregabalin doses were increased based on efficacy and tolerability at each weekly visit.

Arm type	Experimental
Investigational medicinal product name	Pregabalin CR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

Pregabalin CR tablets (82.5 mg-660 mg) were taken for the duration of the single blind for 6 weeks (four weeks dose adjustment, 2 weeks stable dose)

Number of subjects in period 1	Pregabalin CR SB
Started	806
Completed	660
Not completed	146
Unrelated AE	8
Consent withdrawn by subject	29
Unspecified	8
Related adverse event (AE)	46
Lost to follow-up	10
Enrolled but not treated	5

Protocol deviation	8
Lack of efficacy	32

Baseline characteristics

Reporting groups	
Reporting group title	Pregabalin CR SB

Reporting group description: -

Reporting group values	Pregabalin CR SB	Total	
Number of subjects	806	806	
Age categorical Units: Subjects			
<18 years	0	0	
18-44 years	82	82	
45-64 years	300	300	
≥65 years	424	424	
Age continuous Units: years			
arithmetic mean	63.5		
standard deviation	± 13.7	-	
Gender, Male/Female Units: Participants			
Female	458	458	
Male	348	348	

End points

End points reporting groups

Reporting group title	Pregabalin CR SB

Reporting group description:

SB The participants with normal CLcr (≥60 mL/min) were treated with pregabalin 165 mg/day CR; those with low CLcr (>30 - <60 mL/min) received 82.5 mg/day pregabalin CR. Subsequently, the pregabalin doses were increased based on efficacy and tolerability at each weekly visit.

Subject analysis set title	Pregabalin CR DB
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Possible doses for participants with normal creatinine clearance (CLcr) (≥60 mL/min) during the DB fixed dose phase were pregabalin CR 165 mg/day, 330 mg/day, 495 mg/day CR or 660 mg/day CR. Doses for participants with low CLcr (>30 - <60 mL/min) were pregabalin 82.5 mg/day, 165 mg/day, 247.5 mg/day, or 330 mg/day CR.

Subject analysis set title	Placebo DB
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received matching placebo

Primary: Number of participants with loss of therapeutic response.

End point title	Number of participants with loss of therapeutic response.

End point description:

Loss of Therapeutic Response (LTR) is defined as <30% pain response relative to the single blind phase baseline or patient discontinuation due to lack of efficacy or adverse events in the double blind phase of the study. For the calculation of <30% pain response relative to baseline, baseline will be defined as the mean of the last 7 observations prior to the start of SB treatment, which will be compared with the 7 days rolling average of pain response in DB phase. Participants may be discontinued due to lack of efficacy in this study at the discretion of the study physician.

End point type	Primary

End point timeframe:

13 Weeks

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	208	205		
Units: Participants	29	63		

Statistical analyses

Statistical analysis title	Statistical Analysis for participants with LTR

Statistical analysis description:

Kaplan-Meier method was used for the analysis.

Comparison groups	Pregabalin CR DB v Placebo DB

Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank

Secondary: Participants with secondary LTR based on 5 day rolling average diary results

End point title	Participants with secondary LTR based on 5 day rolling average diary results

End point description:

A secondary LTR endpoint (S-LTR) was defined as the 5 day rolling average pain score during DB, compared to the 5 day randomization baseline pain score. As a secondary endpoint, S-LTR was defined as: 1. At least a 30% increase in the 5 days rolling average pain score during DB relative to the 5 Day randomization baseline pain score 2. A 5 days rolling average pain score ≥4. Participants who discontinue due to lack of efficacy or adverse events in the DB phase of the study will also be counted as an LTR.

End point type	Secondary

End point timeframe:

13 Weeks

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	208	205		
Units: Participants	49	87		

Statistical analyses

Statistical analysis title	Analysis for participants with secondary LTR

Statistical analysis description:

Kaplan-Meier method was used for the analysis.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank

Secondary: Percentage of participants with 30% reduction in the mean pain score.

End point title	Percentage of participants with 30% reduction in the mean pain score.

End point description:

The 30% pain responders were defined as participants with at least a 30% reduction in the mean pain

score from SB baseline to DB endpoint.

End point type	Secondary

End point timeframe:

13 Weeks

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	206	204		
Units: Percentage of participants				
number (not applicable)	95.6	83.8		

Statistical analyses

Statistical analysis title	Analysis for 30% reduction in mean pain score

Statistical analysis description:

Chi-square test was used for analysis.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

Secondary: Percentage of participants with 50% reduction in the mean pain score.

End point title	Percentage of participants with 50% reduction in the mean pain score.

End point description:

The 50% pain responders were defined as participants with at least a 50% reduction in the mean pain score from SB baseline to DB endpoint.

End point type	Secondary

End point timeframe:

13 Weeks

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	206	204		
Units: Percentage of participants				
number (not applicable)	88.3	68.6		

Statistical analyses

Statistical analysis title	Analysis for 50% reduction in mean pain score
Statistical analysis description:	
Chi-square test was used for analysis.	
Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

Secondary: Change from Baseline to endpoint in weekly mean pain score.

End point title	Change from Baseline to endpoint in weekly mean pain score.
End point description:	
The pain numeric rating scale (NRS Pain) consists of an 11 point NRS ranging from 0 (no pain) to 10 (worst possible pain). A rating of 1-3 is considered mild pain; 4-6, moderate pain; and 7-10, severe pain	
End point type	Secondary
End point timeframe:	
SB Baseline (Enrollment) to Week 19 and DB Baseline (Week 6) to Week 19	

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	206	205		
Units: Units on a scale				
least squares mean (standard error)				
SB Baseline to Week 19	-4.89 (± 0.12)	-3.95 (± 0.12)		
DB Baseline to Week 19	-0.04 (± 0.11)	0.87 (± 0.11)		

Statistical analyses

Statistical analysis title	Analysis from SB BL to Week 19-mean pain score
Statistical analysis description:	
This ANCOVA model analysis is for SB Baseline to Week 19. Estimates and p-values are from an ANCOVA main effects model with baseline value, pooled center decided before unblinding, and treatment in the model.	
Comparison groups	Pregabalin CR DB v Placebo DB

Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.62
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Analysis from DB BL to Week 19-mean pain score

Statistical analysis description:

This ANCOVA model analysis is for DB Baseline to Week 19. Estimates and p-values are from an ANCOVA main effects model with baseline value, pooled center decided before unblinding, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	-0.61
Variability estimate	Standard error of the mean
Dispersion value	0.15

Secondary: Change in the Weekly NRS-Pain (1-Week Recall).

End point title	Change in the Weekly NRS-Pain (1-Week Recall).

End point description:

The pain numeric rating scale (NRS Pain) consists of an 11 point NRS ranging from 0 (no pain) to 10 (worst possible pain). A rating of 1-3 is considered mild pain; 4-6, moderate pain; and 7-10, severe pain. Participants were asked to rate their pain over the past week.

End point type	Secondary

End point timeframe:

SB Baseline (Enrollment) to Week 19 and DB Baseline (Week 6) to Week 19

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	195		
Units: Units on a scale				
least squares mean (standard error)				
SB Baseline to Week 19	-5 (± 0.13)	-3.9 (± 0.14)		
DB Baseline to Week 19	-0.1 (± 0.13)	0.9 (± 0.13)		

Statistical analyses

Statistical analysis title	Analysis from SB BL to Week 19 for NRS-Pain

Statistical analysis description:

This ANCOVA model analysis is for SB Baseline (BL) to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	-0.75

Statistical analysis title	Analysis from DB BL to Week 19 for NRS-Pain

Statistical analysis description:

This ANCOVA model analysis is for DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	-0.65

Secondary: Change in the Medical Outcomes Study-Sleep Scale (MOS-SS).

End point title	Change in the Medical Outcomes Study-Sleep Scale (MOS-SS).

End point description:

The MOS-SS is a validated self administered questionnaire consisting of 12 items that assess key constructs of sleep. The scale has been found reliable and valid with good overall measurement properties. Instrument scoring yields 7 subscales (sleep disturbance, snoring, awaken short of breath or with a headache, quantity of sleep, optimal sleep, sleep adequacy, and somnolence) as well as a 9 item overall sleep problems index assessing sleep over the past week. Scores are transformed (actual raw score minus lowest possible score divided by possible raw score range multiplied by 100); total score range = 0 to 100; higher score indicates greater intensity of attribute.

End point type	Secondary

End point timeframe:

SB Baseline (BL) (Enrollment) to Week 19 and DB Baseline (Week 6) to Week 19

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	195		
Units: Units on a scale				
least squares mean (standard error)				
Sleep Problems Index I-SB BL to wk 19(N=202,195)	-19.9 (± 1.09)	-16.7 (± 1.13)		
Sleep Problems Index I-DB BL to wk 19(N=202,195)	1.2 (± 1.05)	4.4 (± 1.09)		
SleepProblems Index II-SB BL to wk 19(N=202,195)	-21.2 (± 1.07)	-17.4 (± 1.11)		
SleepProblems Index II-DB BL to wk 19(N=202,194)	0.2 (± 1.01)	4.3 (± 1.05)		
Sleep Disturbance-SB BL to wk 19	-28.31 (± 1.42)	-21.1 (± 1.48)		
Sleep Disturbance-DB BL to wk 19	-1.1 (± 1.31)	7.6 (± 1.36)		
Snoring-SB BL to wk 19(N=202,194)	-3.3 (± 1.57)	-4.7 (± 1.64)		
Snoring-DB BL to wk 19(N=201,194)	-0.6 (± 1.41)	0.8 (± 1.46)		
Awaken short of breath/headache-SB BL to wk 19	-11.9 (± 1.21)	-10.4 (± 1.26)		
Awaken short of breath/headache-DB BL to wk 19	-1.2 (± 1.23)	-0.2 (± 1.27)		
Sleep adequacy-SB BL to wk 19	19.9 (± 1.83)	17.5 (± 1.9)		
Sleep adequacy-DB BL to wk 19(N=202,195)	-3.3 (± 1.82)	-6 (± 1.89)		
Somnolence-SB BL to wk 19(N=202,195)	-12 (± 1.19)	-12 (± 1.23)		
Somnolence-DB BL to wk 19(N=203,194)	-0.7 (± 1.15)	-0.9 (± 1.19)		

Statistical analyses

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Sleep Problem Index I-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0324
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	-0.3

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Sleep Problem Index I-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0223
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	-0.5

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Sleep Problem Index II-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0098
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	-0.9

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Sleep Problem Index II-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0033
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	-1.4

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Sleep Disturbance-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB

Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.1
upper limit	-3.5

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Sleep Disturbance-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	-5.2

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Snoring-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5264
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	5.6

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Snoring-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.452
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	2.3

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Awaken Short of Breath or with a Headache-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3714
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	1.8

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Awaken Short of Breath or with a Headache-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5639
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	2.3

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Sleep adequacy-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3223
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	7.3

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Sleep adequacy-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB

Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2742
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	7.6

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Somnolence-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9816
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	3.1

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Somnolence-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9282
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	3.2

Secondary: Change in the MOS-SS-Quantity of sleep.

End point title	Change in the MOS-SS-Quantity of sleep.

End point description:

The MOS-SS is a validated self administered questionnaire consisting of 12 items that assess key constructs of sleep. The scale has been found reliable and valid with good overall measurement properties. Instrument scoring yields 7 subscales (sleep disturbance, snoring, awaken short of breath or with a headache, quantity of sleep, optimal sleep, sleep adequacy, and somnolence) as well as a 9 item overall sleep problems index assessing sleep over the past week. The item "Quantity of sleep" of MOS-SS is presented here.

End point type	Secondary

End point timeframe:

SB BL (Enrollment) to Week 19 and DB Baseline (Week 6) to Week 19

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	192		
Units: Hours				
least squares mean (standard error)				
Quantity of sleep-SB BL to wk 19(N=203,192)	0.9 (± 0.09)	0.7 (± 0.1)		
Quantity of sleep-DB BL to wk 19(N=202,192)	-0.1 (± 0.08)	-0.4 (± 0.09)		

Statistical analyses

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1635
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.4

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0363
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.5

Secondary: The MOS-SS-Optimal Sleep.

End point title	The MOS-SS-Optimal Sleep.

End point description:

The MOS-SS is a validated self administered questionnaire consisting of 12 items that assess key constructs of sleep. The scale has been found reliable and valid with good overall measurement properties. Instrument scoring yields 7 subscales (sleep disturbance, snoring, awaken short of breath or with a headache, quantity of sleep, optimal sleep, sleep adequacy, and somnolence) as well as a 9 item overall sleep problems index assessing sleep over the past week. The optimal sleep score is a dichotomous 'Yes' or 'No' rating, where 'Yes' indicates optimal sleep (average 7-8 hours per night) and 'No' indicates not optimal sleep. The "percentage of participants with optimal sleep" is presented here.

End point type	Secondary

End point timeframe:

Week 6 and Week 19

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	208	205		
Units: Percentage of participants				
number (not applicable)				
Week 6 (N=208,205)	58.7	62.4		
Week 19 (N=204,197)	54.9	54.8		

Statistical analyses

Statistical analysis title	Statistical Analysis for Week 6 Optimal sleep
Statistical analysis description: This analysis is for Week 6	
Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.432
Method	Chi-squared

Statistical analysis title	Statistical Analysis for Week 19 Optimal sleep
Statistical analysis description: This analysis is for Week 19	
Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.987
Method	Chi-squared

Secondary: Number of participants with change in the Patient Global Impression of Change (PGIC) score

End point title	Number of participants with change in the Patient Global Impression of Change (PGIC) score
End point description: The PGIC is a participant-rated instrument that has been used in chronic pain and fibromyalgia studies to rate change in a patient's overall status. This single item instrument uses a 7 point Likert scale, anchored by (1) very much improved, to (7) very much worse.	
End point type	Secondary
End point timeframe: Week 19	

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	195		
Units: Participants				
Very much improved	64	45		
Much improved	75	59		
Minimally improved	34	37		
No change	21	25		
Minimally worse	5	14		
Much worse	3	14		
Very much worse	1	1		

Statistical analyses

Statistical analysis title	Statistical Analysis for PGIC original score

Statistical analysis description:

This analysis is for the original score. Proportional odds Logistic regression with a term for treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2.65

Statistical analysis title	Statistical Analysis for PGIC categorized score

Statistical analysis description:

This analysis is for the categorized score. Proportional odds Logistic regression with a term for treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0009
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.32

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	3.81

Secondary: Change in the Short Form 36 Health Survey (SF-36)

End point title	Change in the Short Form 36 Health Survey (SF-36)

End point description:

The SF 36 is a self administered, validated questionnaire that measures each of the following 8 health aspects: Physical functioning, role limitations due to physical problems, social functioning, bodily pain, mental health, role limitations due to emotional problems, vitality, and general health perception over the past week. Higher scores indicate a better health related quality of life. The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning) where, higher scores indicate a better health related quality of life.

End point type	Secondary

End point timeframe:

Week 19

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	195		
Units: Units on a scale				
least squares mean (standard error)				
Physical Component-SB BL to wk 19(N=202,195)	7.5 (± 0.54)	5.6 (± 0.56)		
Physical Component-DB BL to wk 19(N=202,195)	0.1 (± 0.51)	-2.3 (± 0.53)		
Mental Component-SB BL to wk 19(N=202,195)	6.4 (± 0.62)	5.5 (± 0.64)		
Mental Component-DB BL to wk 19(N=202,195)	-1.1 (± 0.62)	-2.2 (± 0.64)		
Physical functioning-SB BL to wk 19	11.7 (± 1.44)	8.9 (± 1.49)		
Physical functioning-DB BL to wk 19	-1.4 (± 1.25)	-4.9 (± 1.29)		
Role-Physical-SB BL to wk 19	18.9 (± 1.62)	13.9 (± 1.67)		
Role-Physical-DB BL to wk 19	-2.4 (± 1.54)	-7.7 (± 1.6)		
Bodily pain-SB BL to wk 19	31 (± 1.51)	23.6 (± 1.56)		
Bodily pain-DB BL to wk 19	1.4 (± 1.38)	-6.2 (± 1.43)		
General HealthPerception-SB BL to wk19(N=202,195)	11.3 (± 1.05)	8.2 (± 1.08)		
General HealthPerception-DB BL to wk19(N=202,195)	1.4 (± 0.96)	-4 (± 1)		
Vitality-SB BL to wk 19(N=202,195)	13.7 (± 1.25)	10.7 (± 1.3)		
Vitality-DB BL to wk 19(N=202,195)	-3.5 (± 1.21)	-6.5 (± 1.25)		
Social Functioning-SB BL to wk 19	18.5 (± 1.35)	15.7 (± 1.39)		
Social Functioning-DB BL to wk 19	-2.1 (± 1.28)	-4.3 (± 1.32)		
Role-Emotional-SB BL to wk 19	15 (± 1.43)	11.6 (± 1.47)		
Role-Emotional-DB BL to wk 19	-1.4 (± 1.42)	-5.4 (± 1.47)		

Mental Health-SB BL to wk 19(N=202,195)	11.1 (± 1.05)	9.5 (± 1.08)		
Mental Health-DB BL to wk 19(N=202,195)	-1.3 (± 1.04)	-3.7 (± 1.08)		

Statistical analyses

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Bodily pain-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.4
upper limit	11.5

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Bodily pain-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	11.3

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for General Health Perceptions-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0275
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	6

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for General Health Perceptions-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	8

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Vitality-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB

Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0735
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	6.4

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Vitality-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0684
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	6.2

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Social Functioning-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1197
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	6.4

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Social Functioning-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.221
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	5.5

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Role-Emotional-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0847
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	7.1

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Role-Emotional-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0365
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	7.8

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Mental Health-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2749
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	4.3

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Mental Health-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB

Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0806
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	5.2

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Physical component-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0082
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	3.4

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Physical component-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	3.7

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Mental component-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2097
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	2.5

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Mental component-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1669
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	2.8

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Physical functioning-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1466
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	6.7

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Physical functioning-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0439
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	6.7

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Role-Physical-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB

Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	9.3

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Role-Physical-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0107
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	9.5

Secondary: Change in Mean Daily Sleep Interference scores

End point title	Change in Mean Daily Sleep Interference scores

End point description:

The pain related sleep interference item rating scale is scored on an 11 point numeric rating scale (NRS Sleep). It is self administered by the subject in order to rate how pain has interfered with their sleep during the past 24 hours, ranging from 0 (pain does not interfere with sleep) to 10 (completely interferes (unable to sleep due to pain)). Participants are to describe how their pain has interfered with their sleep during the past 24 hours by choosing the appropriate number on the numeric rating scale.

End point type	Secondary

End point timeframe:

Week 19

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	206	204		
Units: Units on a scale				
least squares mean (standard error)				
SB Baseline to Week 19 (N=205,203)	-4.5 (± 0.11)	-3.5 (± 0.11)		
DB Baseline to Week 19 (N=206,204)	-0.2 (± 0.1)	0.7 (± 0.1)		

Statistical analyses

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with baseline value, pooled center decided before unblinding, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	-0.58

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with baseline value, pooled center decided before unblinding, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	-0.64

Secondary: Change in Hospital Anxiety and Depression Scales (HADS)

End point title	Change in Hospital Anxiety and Depression Scales (HADS)

End point description:

The HADS is a self administered questionnaire that was designed to screen for the presence of a mood disorder in medically ill patients. To distinguish psychiatric presentations from physical illness, the items focus on subjective disturbance of mood rather than physical signs. The HADS contains 14 items rated on 4 point Likert type scales. Two subscales assess depression and anxiety. Each subscale consists of 7 statements, rated on a scale of 0 to 3 (0 = No anxiety or depression, to 3 = Severe feelings of anxiety or depression). Separate scores are calculated for each subscale ranging from 0 to 21. Higher scores denote greater severity of depression or anxiety

End point type	Secondary

End point timeframe:

Week 19

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	195		
Units: Units on a scale				
least squares mean (standard error)				
HADS-Anxiety-SB Baseline to Week 19	-1.8 (± 0.21)	-1.1 (± 0.21)		
HADS-Anxiety-DB Baseline to Week 19	0.1 (± 0.19)	0.9 (± 0.2)		
HADS-Depression-SB Baseline to Week 19	-1.8 (± 0.2)	-1.2 (± 0.21)		
HADS-Depression-DB Baseline to Week 19	0.2 (± 0.19)	0.8 (± 0.19)		

Statistical analyses

Statistical analysis title	Analysis from SB Baseline to Week 19 for Anxiety

Statistical analysis description:

This ANCOVA model analysis is for HADS-Anxiety-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0154
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.1

Statistical analysis title	Analysis from DB Baseline to Week 19 for Anxiety

Statistical analysis description:

This ANCOVA model analysis is for HADS-Anxiety-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0027
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.3

Statistical analysis title	Analysis from SB Baseline to wk 19 for Depression

Statistical analysis description:

This ANCOVA model analysis is for HADS-Depression-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0166
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.1

Statistical analysis title	Analysis from DB Baseline to wk 19 for Depression

Statistical analysis description:

This ANCOVA model analysis is for HADS-Depression-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0217
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.1

Secondary: Change in the Brief Pain Inventory (BPI-sf)

End point title	Change in the Brief Pain Inventory (BPI-sf)

End point description:

The BPI sf is a self-administered questionnaire developed to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation. The BPI sf consists of 5 questions. Questions 1, 2, 3, and 4 measure pain on an 11 point scale from 0 (no pain) to 10 (worst pain possible). Question 5 consists of 7 item subsets which measure the level of interference of pain on daily functions on an 11 point scale from 0 (Does not interfere) to 10 (Completely interferes).

End point type	Secondary

End point timeframe:

Week 19

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	195		
Units: Units on a scale				
least squares mean (standard error)				
Pain Severity Index-SB Baseline to Week 19	-18 (± 0.47)	-13.8 (± 0.49)		
Pain Severity Index-DB Baseline to Week 19	-0.7 (± 0.43)	3.1 (± 0.44)		
Pain Interference Index-SB Baseline to Week 19	-21.9 (± 0.71)	-17.2 (± 0.74)		
Pain Interference Index-DB Baseline to Week 19	-0.2 (± 0.67)	4 (± 0.7)		

Statistical analyses

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Pain Severity Index-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.5
upper limit	-3

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Pain Severity Index-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	-2.7

Statistical analysis title	Analysis from SB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Pain Interference Index-SB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB

Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	-2.7

Statistical analysis title	Analysis from DB BL to Week 19

Statistical analysis description:

This ANCOVA model analysis is for Pain Interference Index-DB Baseline to Week 19. Estimates and p-values are from an analysis of covariance main effects model with SB baseline value, center, and treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	-2.4

Secondary: Percentage of participants with benefit from treatment, satisfaction with treatment and willingness to continue treatement (BSW)

End point title	Percentage of participants with benefit from treatment, satisfaction with treatment and willingness to continue treatement (BSW)

End point description:

The BSW is administered by the study physician or designated site personnel and consists of three single item measures designed to capture the patient's perception of the effect of treatment in terms of the relative benefit, their satisfaction, and their intention or willingness to continue on therapy.

End point type	Secondary

End point timeframe:

Week 19

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	201	193		
Units: Percentage of participants				
number (not applicable)				
Benefit from treatment	98.5	93.3		
Satisfaction with treatment	96	90.7		
Willingness to continue treatment	87.6	81.3		

Statistical analyses

Statistical analysis title	Statistical Analysis for 'Benefit from treatment'

Statistical analysis description:

This analysis is for 'Benefit from treatment'. Proportional odds logistic regression was used with a term for treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0161
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.34
upper limit	17

Statistical analysis title	Analysis for 'Satisfaction with treatment'

Statistical analysis description:

This analysis is for 'Satisfaction with treatment'. Proportional odds logistic regression was used with a term for treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0378
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	5.85

Statistical analysis title	Analysis for 'Willingness to continue treatment'

Statistical analysis description:

This analysis is for 'Willingness to continue treatment'. Proportional odds logistic regression was used with a term for treatment in the model.

Comparison groups	Pregabalin CR DB v Placebo DB
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0901
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	2.81

Secondary: Number of participants with adverse events

End point title	Number of participants with adverse events

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical investigation participant administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. A serious adverse event is any untoward medical occurrence at any dose that: Results in death; Is life-threatening (immediate risk of death); Requires inpatient hospitalization or prolongation of existing hospitalization; Results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); or Results in congenital anomaly/birth defect. The study physician used
the adjective "severe" to those AEs that interfere significantly with participant's usual function.

End point type	Secondary

End point timeframe:

Baseline to Week 20

End point values	Pregabalin CR SB	Pregabalin CR DB	Placebo DB	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	801[1]	208	205	
Units: Participants				
Participants with AEs	441	80	63	
Participants with Serious AEs	17	7	3	
Participants with Severe AEs	35	9	3	

Notes:

[1] - 801 participants were treated

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with suicidal behaviour/ideation

End point title	Percentage of participants with suicidal behaviour/ideation

End point description:

Percentage of participants with suicidal behavior/ideation were noted as Baseline, Weeks 6, 11, 15, 19 and 20.

End point type	Secondary

End point timeframe:

Baseline, Weeks 6, 11, 15, 19 and 20

End point values	Pregabalin CR DB	Placebo DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	208	205		
Units: Percentage of participants				
number (not applicable)				
SB BL(N=208,205)	0	0.5		
Week 6 (N=208,205)	0	0		
Week 11 (N=194,178)	0	0		
Week 15 (N=183,167)	0	0		
Week 19 (N=204,197)	0	0		
Week 20 (N=199,194)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to Week 20

Adverse event reporting additional description:

The SB analysis set (SBAS) consisted of all participants who were enrolled into the SB phase of the study and received at least 1 dose of study medication; The FAS consisted of all participants randomized to the DB phase who received at least 1 dose of study medication in the DB phase. Both SBAS and FAS were included in this analysis.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Pregabalin CR DB

Reporting group description:

Possible doses for participants with normal creatinine clearance (CLcr) (≥60 mL/min) during the DB fixed dose phase were pregabalin CR 165 mg/day, 330 mg/day, 495 mg/day CR or 660 mg/day CR. Doses for participants with low CLcr (>30 - <60 mL/min) were pregabalin 82.5 mg/day, 165 mg/day, 247.5 mg/day, or 330 mg/day CR.

Reporting group title	Placebo DB

Reporting group description:

Participants received matching placebo

Reporting group title	Pregabalin CR SB

Reporting group description:

The participants with normal CLcr (≥60 mL/min) were treated with pregabalin 165 mg/day CR; those with low CLcr (>30 - <60 mL/min) received 82.5 mg/day pregabalin CR. Subsequently, the pregabalin doses were increased based on efficacy and tolerability at each weekly visit.

Serious adverse events	Pregabalin CR DB	Placebo DB	Pregabalin CR SB
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 208 (3.37%)	3 / 205 (1.46%)	17 / 801 (2.12%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Sexual abuse			

subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count increased			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			

subjects affected / exposed	1 / 208 (0.48%)	0 / 205 (0.00%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular disorder			
subjects affected / exposed	0 / 208 (0.00%)	1 / 205 (0.49%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sciatica			
subjects affected / exposed	1 / 208 (0.48%)	0 / 205 (0.00%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia of chronic disease			
subjects affected / exposed	1 / 208 (0.48%)	0 / 205 (0.00%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	0 / 208 (0.00%)	1 / 205 (0.49%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal mass			
subjects affected / exposed	1 / 208 (0.48%)	0 / 205 (0.00%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 208 (0.48%)	0 / 205 (0.00%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 208 (0.48%)	0 / 205 (0.00%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 208 (0.00%)	1 / 205 (0.49%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			

subjects affected / exposed	1 / 208 (0.48%)	0 / 205 (0.00%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 208 (0.00%)	0 / 205 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Pregabalin CR DB	Placebo DB	Pregabalin CR SB
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 208 (3.37%)	1 / 205 (0.49%)	202 / 801 (25.22%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 208 (3.37%)	1 / 205 (0.49%)	137 / 801 (17.10%)
occurrences (all)	7	1	161
Somnolence			

subjects affected / exposed occurrences (all)	1 / 208 (0.48%) 1	0 / 205 (0.00%) 0	91 / 801 (11.36%) 104

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2010	The protocol was amended based on the response received from FDA after request for advice/information. Few of the changes are listed as follows: changes were made in secondary endpoint and information of interim analysis was added. The amendment provided a better understanding of the pharmacokinetic profile.
11 November 2010	The FDA guidance required monitoring of suicidality in all clinical visits, PK section was clarified, edema was added as assessment as part of the physical exam, and changes were made in document history.
16 March 2011	Based on the request by the regulatories changes were made. Few of the changes are listed as follows: the protocol synopsis was added, pregnancy as withdrawal criteria was added, change of suicidality assessment from Suicidality Tracking Scale (STS) to Columbia Suicidal Severity Rating Scale (C SSRS) were made.
18 December 2012	Few of the changes are listed below: The 5 day rolling average during DB, compared to the 5 day randomization baseline pain score was added; medication error are reportable events regardless of whether or not it is accompanied by an AE should be documented; clarification on pregnancy test; and revisions in adverse event sections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported