



## 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:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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 ( $\geq 60$  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:<br>SB The participants with normal CLcr ( $\geq 60$ 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:<br>Possible doses for participants with normal creatinine clearance (CLcr) ( $\geq 60$ 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:<br>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:<br>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:<br>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:<br>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:<br>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 $\geq 4$ . Participants who discontinued 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:<br>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:<br>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:<br>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

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Analysis for 50% reduction in mean pain score |
| Statistical analysis description:<br>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:<br>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:<br>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

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Analysis from SB BL to Week 19-mean pain score |
| Statistical analysis description:<br>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                           |

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | 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 ( $\pm$ 0.13)     | -3.9 ( $\pm$ 0.14)   |  |  |
| DB Baseline to Week 19              | -0.1 ( $\pm$ 0.13)   | 0.9 ( $\pm$ 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:  |  |
| <p>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.</p> |  |
| 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

|  |                                |
|--|--------------------------------|
| <b>Statistical analysis title</b>  | 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                           |

|  |                                |
|--|--------------------------------|
| <b>Statistical analysis title</b>  | 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                           |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | Analysis from SB BL to Week 19 |
|-----------------------------------|--------------------------------|

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**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                           |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                           |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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     |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | Analysis from DB BL to Week 19 |
|-----------------------------------|--------------------------------|

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**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

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**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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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, awoken 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     |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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, awoken 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

|  |   |
|--|---|
| <b>Statistical analysis title</b>                                | Statistical Analysis for Week 6 Optimal sleep |
| Statistical analysis description:<br>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                                   |

|   |  |
|---|--|
| <b>Statistical analysis title</b>                                 | Statistical Analysis for Week 19 Optimal sleep |
| Statistical analysis description:<br>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:<br>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:<br>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:  |   |
| <p>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.</p> |   |
| 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 ( $\pm$ 1.05) | 9.5 ( $\pm$ 1.08)  |  |  |
| Mental Health-DB BL to wk 19(N=202,195) | -1.3 ( $\pm$ 1.04) | -3.7 ( $\pm$ 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                              |

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**Statistical analysis title**

Analysis from DB BL to Week 19

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**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                              |

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**Statistical analysis title**

Analysis from SB BL to Week 19

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**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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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     |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | Analysis from DB BL to Week 19 |
|-----------------------------------|--------------------------------|

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**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                            |

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**Statistical analysis title**

Analysis from SB BL to Week 19

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**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                            |

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**Statistical analysis title**

Analysis from DB BL to Week 19

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**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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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     |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | Analysis from SB BL to Week 19 |
|-----------------------------------|--------------------------------|

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**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                            |

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**Statistical analysis title**

Analysis from DB BL to Week 19

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**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                            |

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**Statistical analysis title**

Analysis from SB BL to Week 19

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**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                            |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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 ( $\pm$ 0.11)   | -3.5 ( $\pm$ 0.11)   |  |  |
| DB Baseline to Week 19 (N=206,204)  | -0.2 ( $\pm$ 0.1)    | 0.7 ( $\pm$ 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    |

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | 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                           |

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | 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                           |

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | 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:   |   |
| <p>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).</p> |   |
| 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**

|  |                                |
|--|--------------------------------|
| <b>Statistical analysis title</b>  | 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                             |

|  |                                |
|--|--------------------------------|
| <b>Statistical analysis title</b>  | 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                           |

|  |                                |
|--|--------------------------------|
| <b>Statistical analysis title</b>  | 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                           |

|                                   |                                |
|-----------------------------------|--------------------------------|
| <b>Statistical analysis title</b> | 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 treatment (BSW)**

|                 |   |
|-----------------|---|
| End point title | Percentage of participants with benefit from treatment, satisfaction with treatment and willingness to continue treatment (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

| <b>End point values</b>           | 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

| <b>Statistical analysis title</b>   | 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  |

| <b>Statistical analysis title</b>  | 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                                       |



|  |  |
|--|--|
| <b>Statistical analysis title</b>  | 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 <sup>[1]</sup> | 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) ( $\geq 60$  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 ( $\geq 60$  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                      |                 |                 |                 |
| Gastroesophageal 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 | 1 / 208 (0.48%) | 0 / 205 (0.00%) | 91 / 801 (11.36%) |
| occurrences (all)           | 1               | 0               | 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 regulatory 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:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported