



## Clinical trial results:

### A 6-MONTH, OPEN-LABEL, SAFETY TRIAL OF PREGABALIN IN ADOLESCENT PATIENTS WITH FIBROMYALGIA

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2010-020300-29 |
| Trial protocol           | CZ             |
| Global end of trial date | 01 June 2015   |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 24 February 2016 |
| First version publication date | 24 February 2016 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | A0081231 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01020526 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Pfizer, Inc.  |
| Sponsor organisation address | 235 East 42nd Street, New York, NY, United States, 10017  |
| Public contact               | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact           | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 800-718-1021, 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? | Yes |

Notes:

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**Results analysis stage**

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 24 September 2015 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 01 June 2015      |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 01 June 2015      |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

Main objective of the trial:

To evaluate the safety of pregabalin at doses of 75-450 mg/day (taken in twice daily [BID] doses) in participants who participated in the double-blind fibromyalgia study A0081180 and who wished to receive open-label pregabalin therapy.

Protection of trial subjects:

The study was conducted in accordance with the protocol, 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), Guidelines for Good Clinical Practice (GCP) (International Conference on Harmonization [ICH] 1996), and the Declaration of Helsinki (World Medical Association 1996 and 2008). In addition, the study was conducted in accordance with applicable local regulatory requirements and laws.

Background therapy:

This study has no background medication therapy.

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 01 September 2010 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

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**Population of trial subjects****Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 40 |
| Country: Number of subjects enrolled | India: 20         |
| Country: Number of subjects enrolled | Czech Republic: 3 |
| Worldwide total number of subjects   | 63                |
| EEA total number of subjects         | 3                 |

Notes:

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**Subjects enrolled per age group**

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

|                           |    |
|---------------------------|----|
| Adolescents (12-17 years) | 63 |
| Adults (18-64 years)      | 0  |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 63 participants were screened and enrolled at 19 study centers in this open-label extension study to the parent double-blind randomized fibromyalgia study A0081180.

### Pre-assignment

Screening details:

Participants initiated dosing at 75 mg/day and their dose was optimized over a 3 week period, based on tolerability and response, to a dose of 75 mg/day, 150 mg/day, 300 mg/day or 450 mg/day.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Non-randomised - controlled    |
| Blinding used                | Not blinded                    |

### Arms

|           |            |
|-----------|------------|
| Arm title | Pregabalin |
|-----------|------------|

Arm description:

Participants initiated dosing at 75 mg/day, and their dose was optimized over a 3 week period based on tolerability and response to a dose of 75 mg/day, 150 mg/day, 300 mg/day or 450 mg/day. These doses were administered during the subsequent flexible dosing phase for a period of 21 weeks. Pregabalin was administered orally as capsules.

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Lyrica        |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

75 mg/day to 450 mg/day

| Number of subjects in period 1 | Pregabalin |
|--------------------------------|------------|
| Started                        | 63         |
| Completed                      | 49         |
| Not completed                  | 14         |
| Consent withdrawn by subject   | 5          |
| Adverse event, non-fatal       | 2          |
| Other reasons                  | 3          |
| Lost to follow-up              | 1          |
| Insufficient clinical response | 3          |

## Baseline characteristics

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Pregabalin |
|-----------------------|------------|

Reporting group description:

Participants initiated dosing at 75 mg/day, and their dose was optimized over a 3 week period based on tolerability and response to a dose of 75 mg/day, 150 mg/day, 300 mg/day or 450 mg/day. These doses were administered during the subsequent flexible dosing phase for a period of 21 weeks. Pregabalin was administered orally as capsules.

| Reporting group values                                | Pregabalin | Total |  |
|---|------------|-------|--|
| Number of subjects                                    | 63         | 63    |  |
| Age categorical                                       |            |       |  |
| Units: Subjects                                       |            |       |  |
| In utero  | 0          | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0          | 0     |  |
| Newborns (0-27 days)                                  | 0          | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0          | 0     |  |
| Children (2-11 years)                                 | 0          | 0     |  |
| Adolescents (12-17 years)                             | 63         | 63    |  |
| Adults (18-64 years)                                  | 0          | 0     |  |
| From 65-84 years                                      | 0          | 0     |  |
| 85 years and over                                     | 0          | 0     |  |
| Age Continuous   Male                                 |            |       |  |
| Units: years  |            |       |  |
| arithmetic mean                                       | 14.8       |       |  |
| standard deviation                                    | ± 1.4      | -     |  |
| Gender, Male/Female                                   |            |       |  |
| Units: Participants                                   |            |       |  |
| Female  | 53         | 53    |  |
| Male  | 10         | 10    |  |

## End points

### End points reporting groups

|  |            |
|--|------------|
| Reporting group title  | Pregabalin |
| Reporting group description:   |            |
| Participants initiated dosing at 75 mg/day, and their dose was optimized over a 3 week period based on tolerability and response to a dose of 75 mg/day, 150 mg/day, 300 mg/day or 450 mg/day. These doses were administered during the subsequent flexible dosing phase for a period of 21 weeks. Pregabalin was administered orally as capsules. |            |

### Primary: Change from baseline in pain numeric rating scale by week

|  |  |
|--|--|
| End point title  | Change from baseline in pain numeric rating scale by week <sup>[1]</sup> |
| End point description:   |  |
| The weekly pain numeric rating scale (Weekly Pain NRS) consists of an 11-point NRS ranging from 0 (no pain) to 10 (worst possible pain), where higher scores indicate worse pain. Participants chose the number that best described the pain during the last week. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| Baseline, Weeks 3, 8, 16, 24 and Last Visit.   |  |

Notes:

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

Justification: No statistical analyses were planned for this primary endpoint

| End point values                     | Pregabalin      |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 63              |  |  |  |
| Units: Units on a Scale              |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| Baseline (N=63)                      | 6.7 (± 1.68)    |  |  |  |
| Week 3 (N=61)                        | -2.1 (± 2.51)   |  |  |  |
| Week 8 (N=55)                        | -1.8 (± 2.95)   |  |  |  |
| Week 16 (N=51)                       | -2.1 (± 2.6)    |  |  |  |
| Week 24 (N=55)                       | -2.1 (± 2.56)   |  |  |  |
| Last Visit (N=63)                    | -2.1 (± 2.47)   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All adverse events were recorded from the time the participants had taken at least 1 dose of study drug through the last subject visit.

Adverse event reporting additional description:

For summary purposes, adverse event investigator terms were converted to preferred terms using a standard system of classification (COSTART or MedDRA). Adverse events tabulations included summaries by body system or system organ class, by overall decreasing frequency and by maximum intensity.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 18.0   |

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Pregabalin |
|-----------------------|------------|

Reporting group description:

Participants initiated dosing at 75 mg/day and their dose was optimized over a 3 week period, based on tolerability and response, to a dose of 75 mg/day, 150 mg/day, 300 mg/day or 450 mg/day.

| Serious adverse events                            | Pregabalin     |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 3 / 63 (4.76%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |
| Nervous system disorders                          |                |  |  |
| Migraine  |                |  |  |
| subjects affected / exposed                       | 1 / 63 (1.59%) |  |  |
| occurrences causally related to treatment / all   | 1 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders   |                |  |  |
| Joint instability                                 |                |  |  |
| subjects affected / exposed                       | 1 / 63 (1.59%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| Infections and infestations                       |                |  |  |
| Appendicitis                                      |                |  |  |
| subjects affected / exposed                       | 1 / 63 (1.59%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                     | Pregabalin       |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 32 / 63 (50.79%) |  |  |
| Nervous system disorders                              |                  |  |  |
| Dizziness   |                  |  |  |
| subjects affected / exposed                           | 14 / 63 (22.22%) |  |  |
| occurrences (all)                                     | 16               |  |  |
| Headache  |                  |  |  |
| subjects affected / exposed                           | 6 / 63 (9.52%)   |  |  |
| occurrences (all)                                     | 10               |  |  |
| General disorders and administration site conditions  |                  |  |  |
| Fatigue   |                  |  |  |
| subjects affected / exposed                           | 8 / 63 (12.70%)  |  |  |
| occurrences (all)                                     | 11               |  |  |
| Gastrointestinal disorders                            |                  |  |  |
| Abdominal pain  |                  |  |  |
| subjects affected / exposed                           | 5 / 63 (7.94%)   |  |  |
| occurrences (all)                                     | 5                |  |  |
| Abdominal pain upper                                  |                  |  |  |
| subjects affected / exposed                           | 5 / 63 (7.94%)   |  |  |
| occurrences (all)                                     | 6                |  |  |
| Nausea  |                  |  |  |
| subjects affected / exposed                           | 5 / 63 (7.94%)   |  |  |
| occurrences (all)                                     | 7                |  |  |
| Reproductive system and breast disorders              |                  |  |  |
| Dysmenorrhoea   |                  |  |  |
| subjects affected / exposed                           | 3 / 63 (4.76%)   |  |  |
| occurrences (all)                                     | 4                |  |  |
| Respiratory, thoracic and mediastinal disorders       |                  |  |  |



|   |                     |  |  |
|---|---------------------|--|--|
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)                  | 4 / 63 (6.35%)<br>4 |  |  |
| Infections and infestations   |                     |  |  |
| Ear infection<br>subjects affected / exposed<br>occurrences (all)                     | 4 / 63 (6.35%)<br>4 |  |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 4 / 63 (6.35%)<br>6 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 31 December 2012 | Updated Pfizer protocol template wording was implemented. Information regarding the importance of parent/guardian/caregiver involvement in overseeing subject participation, especially dosing, was added. |
| 14 March 2014    | The Columbia Suicide Severity Rating Scale (C-SSRS) was added as a required study assessment.  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported