



## Clinical trial results:

### **A 6-Month, Open-Label, Prospective, Multicenter, International, Exploratory Study of a Transition to Flexibly-Dosed Paliperidone Palmitate in Patients with Schizophrenia Previously Unsuccessfully Treated with Oral or Long-Acting Injectable Antipsychotics**

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

#### Summary

|                          |   |
|--------------------------|---|
| EudraCT number           | 2009-018022-30                            |
| Trial protocol           | PT HU DE NL BE ES GB SE DK IT LV AT EE LT |
| Global end of trial date | 29 November 2013                          |

#### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 15 July 2016   |
| First version publication date | 15 August 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li><li>• Review of data</li></ul> |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | R092670SCH3010 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01281527 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Janssen-Cilag International NV   |
| Sponsor organisation address | Turnhoutseweg 30, 2340 Beerse, Belgium,  |
| Public contact               | Janssen-Cilag International NV, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Janssen-Cilag International NV, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.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                       | 29 November 2013 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 29 November 2013 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to explore the tolerability, safety and treatment response (maintained/improved efficacy); based on total Positive and Negative Syndrome Scale (PANSS) score, following a transition to flexibly dosed once-monthly paliperidone palmitate (PP) in subjects with schizophrenia previously unsuccessfully treated with oral or long-acting injectable (LAI) antipsychotics. Subjects with either acute or non-acute symptoms of schizophrenia were eligible to enter the study.

Protection of trial subjects:

Safety and tolerability were monitored by evaluating adverse events, vital signs, physical examination, body weight/body mass index (BMI), and assessment of extrapyramidal symptoms (using the Extrapyramidal Symptom Rating Scale [ESRS]), and urine pregnancy test.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 02 November 2010 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Austria: 11        |
| Country: Number of subjects enrolled | Belgium: 67        |
| Country: Number of subjects enrolled | Netherlands: 5     |
| Country: Number of subjects enrolled | Croatia: 4         |
| Country: Number of subjects enrolled | Denmark: 5         |
| Country: Number of subjects enrolled | Estonia: 9         |
| Country: Number of subjects enrolled | France: 82         |
| Country: Number of subjects enrolled | Germany: 114       |
| Country: Number of subjects enrolled | United Kingdom: 34 |
| Country: Number of subjects enrolled | Greece: 27         |
| Country: Number of subjects enrolled | Hungary: 18        |
| Country: Number of subjects enrolled | Israel: 17         |
| Country: Number of subjects enrolled | Italy: 123         |
| Country: Number of subjects enrolled | Latvia: 56         |
| Country: Number of subjects enrolled | Lithuania: 8       |

|                                      |                 |
|--------------------------------------|-----------------|
| Country: Number of subjects enrolled | Portugal: 32    |
| Country: Number of subjects enrolled | Spain: 170      |
| Country: Number of subjects enrolled | Sweden: 16      |
| Country: Number of subjects enrolled | Switzerland: 10 |
| Country: Number of subjects enrolled | Turkey: 78      |
| Country: Number of subjects enrolled | Ukraine: 149    |
| Worldwide total number of subjects   | 1035            |
| EEA total number of subjects         | 781             |

Notes:

---

### **Subjects enrolled per age group**

|   |      |
|---|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 1    |
| Adults (18-64 years)                      | 1009 |
| From 65 to 84 years                       | 25   |
| 85 years and over                         | 0    |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study consisted of a screening period, a 6-month study period, and an optional open-label extension phase. 3 groups of subjects were pre-specified with schizophrenia who transitioned to PP: Group A (600 non-acute) and C (200 acute)- subjects switched due to oral antipsychotics; Group B(200 non-acute)- subjects switched due to LAI antipsychotic.

### 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

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Group A |
|------------------|---------|

Arm description:

Group A included approximately 600 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with an oral anti psychotic in the 4 weeks prior to enrollment.

|  |  |
|--|--|
| Arm type                               | Experimental                                   |
| Investigational medicinal product name | Paliperidone palmitate - Extended Release (ER) |
| Investigational medicinal product code | R092670  |
| Other name                             |  |
| Pharmaceutical forms                   | Suspension for injection                       |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

Subjects received intramuscular injection of PP on Day 1 at a dose of 150 milligram equivalent (mg eq.) and their second injection on Day 8 (100 mg eq.). Subsequent injections were given once monthly within the dose range of 50 to 150 mg eq. at the discretion of the investigator.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Group B |
|------------------|---------|

Arm description:

Group B included approximately 200 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with a frequently used LAI anti psychotics (i.e., haloperidol decanoate, flupentixol decanoate, fluphenazine decanoate, zuclopenthixol decanoate, or risperidone LAI) in the 4 weeks prior to enrollment.

|  |  |
|--|--|
| Arm type                               | Experimental                                   |
| Investigational medicinal product name | Paliperidone palmitate - Extended Release (ER) |
| Investigational medicinal product code | R092670  |
| Other name                             |  |
| Pharmaceutical forms                   | Suspension for injection                       |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

Subjects received intramuscular injection of PP on Day 1 with in a range of 50 - 150 mg eq. Subsequent injections were given once monthly within the dose range of 50 to 150 mg eq. at the discretion of the investigator.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Group C |
|------------------|---------|

Arm description:

Group C included approximately 200 subjects with acute symptoms of schizophrenia who were transitioned to PP because of unsuccessful

treatment with an oral antipsychotic in the 4 weeks prior to enrollment.

|  |  |
|--|--|
| Arm type                               | Experimental                                   |
| Investigational medicinal product name | Paliperidone palmitate - Extended Release (ER) |
| Investigational medicinal product code | R092670  |
| Other name                             |  |
| Pharmaceutical forms                   | Suspension for injection                       |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

Subjects received intramuscular injection of PP on Day 1 at a dose of 150 mg eq. and their second injection on Day 8 (100 mg eq.). Subsequent injections were given once monthly within the dose range of 50 to 150 mg eq. at the discretion of the investigator.

| <b>Number of subjects in period 1</b> | Group A | Group B | Group C |
|---------------------------------------|---------|---------|---------|
| Started                               | 593     | 230     | 212     |
| Completed                             | 442     | 172     | 149     |
| Not completed                         | 151     | 58      | 63      |
| Physician decision                    | 8       | 3       | -       |
| Consent withdrawn by subject          | 60      | 19      | 20      |
| Death                                 | 1       | -       | 2       |
| Other                                 | 2       | 3       | 3       |
| Adverse event                         | 36      | 17      | 19      |
| Noncompliance with study drug         | 4       | 2       | 1       |
| Lost to follow-up                     | 19      | 5       | 10      |
| Protocol deviation                    | 6       | 2       | 2       |
| Lack of efficacy                      | 15      | 7       | 6       |

## Baseline characteristics

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Group A |
|-----------------------|---------|

Reporting group description:

Group A included approximately 600 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with an oral anti psychotic in the 4 weeks prior to enrollment.

|                       |         |
|-----------------------|---------|
| Reporting group title | Group B |
|-----------------------|---------|

Reporting group description:

Group B included approximately 200 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with a frequently used LAI anti psychotics (i.e., haloperidol decanoate, flupentixol decanoate, fluphenazine decanoate, zuclopenthixol decanoate, or risperidone LAI) in the 4 weeks prior to enrollment.

|                       |         |
|-----------------------|---------|
| Reporting group title | Group C |
|-----------------------|---------|

Reporting group description:

Group C included approximately 200 subjects with acute symptoms of schizophrenia who were transitioned to PP because of unsuccessful treatment with an oral antipsychotic in the 4 weeks prior to enrollment.

| Reporting group values                      | Group A | Group B | Group C |
|---|---------|---------|---------|
| Number of subjects                          | 593     | 230     | 212     |
| Title for AgeCategorical<br>Units: subjects |         |         |         |
| Children (2-11 years)                       | 0       | 0       | 0       |
| Adolescents (12-17 years)                   | 1       | 0       | 0       |
| Adults (18-64 years)                        | 581     | 220     | 208     |
| From 65 to 84 years                         | 11      | 10      | 4       |
| 85 years and over                           | 0       | 0       | 0       |
| Title for AgeContinuous<br>Units: years     |         |         |         |
| arithmetic mean                             | 38.4    | 42.5    | 36.4    |
| standard deviation                          | ± 11.83 | ± 10.83 | ± 12.06 |
| Title for Gender<br>Units: subjects         |         |         |         |
| Female                                      | 219     | 83      | 87      |
| Male  | 374     | 147     | 125     |

| Reporting group values                      | Total |  |  |
|---|-------|--|--|
| Number of subjects                          | 1035  |  |  |
| Title for AgeCategorical<br>Units: subjects |       |  |  |
| Children (2-11 years)                       | 0     |  |  |
| Adolescents (12-17 years)                   | 1     |  |  |
| Adults (18-64 years)                        | 1009  |  |  |
| From 65 to 84 years                         | 25    |  |  |
| 85 years and over                           | 0     |  |  |
| Title for AgeContinuous<br>Units: years     |       |  |  |
| arithmetic mean                             | -     |  |  |
| standard deviation                          | -     |  |  |

|                  |     |  |  |
|------------------|-----|--|--|
| Title for Gender |     |  |  |
| Units: subjects  |     |  |  |
| Female           | 389 |  |  |
| Male             | 646 |  |  |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Group A   |
| Reporting group description:<br>Group A included approximately 600 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with an oral anti psychotic in the 4 weeks prior to enrollment.  |   |
| Reporting group title  | Group B   |
| Reporting group description:<br>Group B included approximately 200 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with a frequently used LAI anti psychotics (i.e., haloperidol decanoate, flupentixol decanoate, fluphenazine decanoate, zuclopentixol decanoate, or risperidone LAI) in the 4 weeks prior to enrollment. |   |
| Reporting group title  | Group C   |
| Reporting group description:<br>Group C included approximately 200 subjects with acute symptoms of schizophrenia who were transitioned to PP because of unsuccessful treatment with an oral antipsychotic in the 4 weeks prior to enrollment.  |   |
| Subject analysis set title   | Group A1: Subjects Switched for Efficacy Reason           |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:<br>Efficacy analysis set included all Intent-to-treat (ITT) subjects who had at least one post baseline observation on any efficacy parameter.   |   |
| Subject analysis set title   | Group A2: Subjects Switched for Other Reason              |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:<br>Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.   |   |
| Subject analysis set title   | Group B1: Subjects Switched from Haloperidol Decanoate    |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:<br>Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.   |   |
| Subject analysis set title   | Group B2: Subjects Switched from Flupentixol Decanoate    |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:<br>Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.   |   |
| Subject analysis set title   | Group B3: Subjects Switched from Fluphenazine Decanoate   |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:<br>Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.   |   |
| Subject analysis set title   | Group B4: Subjects Switched from Zuclopentixol-Decanoate  |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:<br>Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.   |   |
| Subject analysis set title   | Group B5: Subjects Switched from Risperidone Micropsheres |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:<br>Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.   |   |
| Subject analysis set title   | Group C   |

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Group C included approximately 200 subjects with acute symptoms of schizophrenia who were transitioned to PP because of unsuccessful treatment with an oral antipsychotic in the 4 weeks prior to enrollment.

**Primary: Group A1 (Non acute Patients Switched From oral Anti psychotics due to Lack of Efficacy): Percentage of Participants with Improved Efficacy in PANSS Total Score from Baseline to Month 6 LOCF**

|                 |   |
|-----------------|---|
| End point title | Group A1 (Non acute Patients Switched From oral Anti psychotics due to Lack of Efficacy): Percentage of Participants with Improved Efficacy in PANSS Total Score from Baseline to Month 6 LOCF <sup>[1]</sup> |
|-----------------|---|

End point description:

Improved efficacy, defined as the proportion of patients who showed an improvement in PANSS total score of at  $\geq 20\%$  from baseline to endpoint (LOCF). PANSS is a 30-item scale, with each item rated on a scale of 1 (absent) to 7 (extreme). The PANSS provides a total score (range, 30-210) and scores for the following 3 subscales: positive subscale (range, 7-49): sum of Items P1 to P7 in the positive subscale; negative subscale (range, 7-49): sum of Items N1 to N7 in the negative subscale; general psychopathology subscale (range, 16-112): sum of Items G1 to G16 in the general psychopathology subscale. Efficacy analysis included all subjects who received at least 1 dose of paliperidone palmitate (PP) and had at least 1 post baseline observation on any efficacy parameter.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Month 6 LOCF

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: Descriptive statistics were done, no inferential statistical analyses were performed.

|                                   |   |  |  |  |
|-----------------------------------|---|--|--|--|
| <b>End point values</b>           | Group A1: Subjects Switched for Efficacy Reason |  |  |  |
| Subject group type                | Subject analysis set                            |  |  |  |
| Number of subjects analysed       | 143   |  |  |  |
| Units: percentage of participants |   |  |  |  |
| median (confidence interval 95%)  | 61.5 (53.4 to 69.1)                             |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Group B: (Non-acute Patients Switched From Long Acting Injectable Antipsychotics): Participants with Explore Treatment Response**

|                 |  |
|-----------------|--|
| End point title | Group B: (Non-acute Patients Switched From Long Acting Injectable Antipsychotics): Participants with Explore Treatment Response <sup>[2]</sup> |
|-----------------|--|

End point description:

Participants with explore treatment response switched from Long Acting Injectable (LAI) anti-psychotics (haloperidol decanoate, flupentixol decanoate, fluphenazine decanoate, zuclopenthixol decanoate, risperidone LAI) defined as the proportion of subjects achieving a  $\geq 20\%$  improvement in PANSS total score from baseline to endpoint (LOCF). The PANSS is a 30-item scale, with each item rated on a scale of 1 (absent) to 7 (extreme). The PANSS provides a total score (range, 30-210) and scores for the following 3 subscales: positive subscale (range, 7-49): sum of Items P1 to P7 in the positive subscale; negative subscale (range, 7-49): sum of Items N1 to N7 in the negative subscale; general

psychopathology subscale (range, 16-112): sum of Items G1 to G16 in the general psychopathology subscale. Efficacy analysis included all subjects who received at least 1 dose of study medication (PP) and had at least 1 post baseline observation on any efficacy parameter.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Month 6 LOCF

Notes:

[2] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

| <b>End point values</b>           | Group B1:<br>Subjects<br>Switched from<br>Haloperidol<br>Decanoate | Group B2:<br>Subjects<br>Switched from<br>Flupentixol<br>Decanoate | Group B3:<br>Subjects<br>Switched from<br>Fluphenazine<br>Decanoate | Group B4:<br>Subjects<br>Switched from<br>Zuclopentixol-<br>Decanoate |
|-----------------------------------|--|--|---|---|
| Subject group type                | Subject analysis set   | Subject analysis set   | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed       | 53   | 34   | 44  | 41  |
| Units: Percentage of participants |  |  |   |   |
| median (confidence interval 95%)  | 54.7 (41.4 to<br>67.3)   | 61.8 (45 to<br>76.1)   | 59.1 (44.4 to<br>72.3)  | 53.7 (38.8 to<br>67.9)  |

| <b>End point values</b>           | Group B5:<br>Subjects<br>Switched from<br>Risperidone<br>Micropsheres |  |  |  |
|-----------------------------------|---|--|--|--|
| Subject group type                | Subject analysis set  |  |  |  |
| Number of subjects analysed       | 55  |  |  |  |
| Units: Percentage of participants |   |  |  |  |
| median (confidence interval 95%)  | 61.1 (47.8 to<br>73)  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### **Primary: Group C (Acute Patients Switched From Oral Anti psychotics): Participants with Improved Efficacy From Baseline to Month 6 LOCF**

|                 |  |
|-----------------|--|
| End point title | Group C (Acute Patients Switched From Oral Anti psychotics):<br>Participants with Improved Efficacy From Baseline to Month 6<br>LOCF <sup>[3][4]</sup> |
|-----------------|--|

End point description:

participants with improved efficacy defined as the proportion of patients achieving a  $\geq 30\%$  improvement in PANSS total score from baseline to endpoint (LOCF). The PANSS is a 30-item scale, with each item rated on a scale of 1 (absent) to 7 (extreme). The PANSS provides a total score (range, 30-210) and scores for the following 3 subscales: positive subscale (range, 7-49): sum of Items P1 to P7 in the positive subscale; negative subscale (range, 7-49): sum of Items N1 to N7 in the negative subscale; general psychopathology subscale (range, 16-112): sum of Items G1 to G16 in the general psychopathology subscale. Efficacy analysis included all subjects who received at least 1 dose of paliperidone palmitate (PP) and had at least 1 post baseline observation on any efficacy parameter.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline to Month 6 LOCF

Notes:

[3] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

| <b>End point values</b>           | Group C           |  |  |  |
|-----------------------------------|-------------------|--|--|--|
| Subject group type                | Reporting group   |  |  |  |
| Number of subjects analysed       | 207               |  |  |  |
| Units: Percentage of participants |                   |  |  |  |
| median (confidence interval 95%)  | 66.7 (60 to 72.7) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### **Primary: Group A2 (Non-acute Participants Switched From Oral Anti-psychotics due to Other Reasons): Percentage of Participants With Maintained Efficacy From baseline to Month 6 LOCF**

|                 |   |
|-----------------|---|
| End point title | Group A2 (Non-acute Participants Switched From Oral Anti-psychotics due to Other Reasons): Percentage of Participants With Maintained Efficacy From baseline to Month 6 LOCF <sup>[5]</sup> |
|-----------------|---|

End point description:

Percentage of participants with maintained efficacy, defined as a non-inferior change in PANSS total score from baseline to endpoint based on the Schuirmann's test. PANSS is a 30-item scale, with each item rated on a scale of 1 (absent) to 7 (extreme). The PANSS provides a total score (range, 30-210) and scores for the following 3 subscales: positive subscale (range, 7-49): sum of Items P1 to P7 in the positive subscale; negative subscale (range, 7-49): sum of Items N1 to N7 in the negative subscale; general psychopathology subscale (range, 16-112): sum of Items G1 to G16 in the general psychopathology subscale. Efficacy analysis included all subjects who received at least 1 dose of paliperidone palmitate (PP) and had at least 1 post baseline observation on any efficacy parameter.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Month 6 LOCF

Notes:

[5] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

| <b>End point values</b>           | Group A2: Subjects Switched for Other Reason |  |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                         |  |  |  |
| Number of subjects analysed       | 446  |  |  |  |
| Units: Percentage of participants |  |  |  |  |
| median (confidence interval 95%)  |  |  |  |  |
| Baseline                          | 69 (67.3 to 70)                              |  |  |  |

|                |                      |  |  |  |
|----------------|----------------------|--|--|--|
| Month 6 (LOCF) | -11 (-13.1 to -10.1) |  |  |  |
|----------------|----------------------|--|--|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Clinical Global Impression-Severity Scale [CGI-S] at Month 6

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Clinical Global Impression-Severity Scale [CGI- S] at Month 6 |
|-----------------|---|

End point description:

The Clinical Global Impression-Severity Scale (CGI-S) rating scale is used to rate the severity of a subject's psychotic condition on a 7-point scale ranging from 1 (not ill) to 7 (extremely severe). Efficacy analysis included all subjects who received at least 1 dose of PP and had at least 1 post baseline observation on any efficacy parameter. Here 'n' signifies number of subjects analysed for this endpoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Month 6 LOCF

| End point values                              | Group A1:<br>Subjects<br>Switched for<br>Efficacy Reason | Group A2:<br>Subjects<br>Switched for<br>Other Reason | Group B1:<br>Subjects<br>Switched from<br>Haloperidol<br>Decanoate | Group B2:<br>Subjects<br>Switched from<br>Flupentixol<br>Decanoate |
|---|--|---|--|--|
| Subject group type                            | Subject analysis set                                     | Subject analysis set                                  | Subject analysis set   | Subject analysis set   |
| Number of subjects analysed                   | 143  | 446   | 53   | 34   |
| Units: units on a scale                       |  |   |  |  |
| arithmetic mean (standard deviation)          |  |   |  |  |
| Baseline<br>(n=143,442,53,34,44,41,55,205)    | 4.2 (± 0.89)   | 3.8 (± 0.91)  | 4.2 (± 0.91)   | 3.9 (± 0.77)   |
| Month 6<br>LOCF(n=143,442,53,34,44,41,55,205) | -0.6 (± 0.86)  | -0.6 (± 1.09)   | -0.4 (± 1.1)   | -0.4 (± 0.86)  |

| End point values                              | Group B3:<br>Subjects<br>Switched from<br>Fluphenazine<br>Decanoate | Group B4:<br>Subjects<br>Switched from<br>Zuclopentixol-<br>Decanoate | Group B5:<br>Subjects<br>Switched from<br>Risperidone<br>Micropsheres | Group C              |
|---|---|---|---|----------------------|
| Subject group type                            | Subject analysis set  | Subject analysis set  | Subject analysis set  | Subject analysis set |
| Number of subjects analysed                   | 44  | 41  | 55  | 207                  |
| Units: units on a scale                       |   |   |   |                      |
| arithmetic mean (standard deviation)          |   |   |   |                      |
| Baseline<br>(n=143,442,53,34,44,41,55,205)    | 4 (± 1.03)  | 4.1 (± 1)   | 3.7 (± 1.21)  | 5 (± 0.75)           |
| Month 6<br>LOCF(n=143,442,53,34,44,41,55,205) | -0.4 (± 0.94)   | -0.5 (± 1.19)   | -0.4 (± 1.19)   | -1.5 (± 1.27)        |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Personal And Social Functioning (Personal and Social Performance Scale [PSP]) at Month 6

|                        |  |
|------------------------|--|
| End point title        | Change from Baseline in Personal And Social Functioning (Personal and Social Performance Scale [PSP]) at Month 6   |
| End point description: | The PSP scale was used to assess the degree of functioning a subject exhibited within 4 domains: a) socially useful activities, b) personal and social relationships, c) self-care, and d) disturbing and aggressive behavior. Each of the 4 domains was rated on a 6-point scale (0=absent, 1=mild, 2=manifest, 3=marked, 4=severe, and 5=very severe) and then converted to one total score (ranging from 1 to 100). A total PSP score of 71 to 100 indicated a mild degree of difficulty; a score of 31 to 70 indicated varying degrees of disability; and a score 30 indicated functioning so poor that the subject requires intensive support or supervision. Efficacy analysis included all subjects who received at least 1 dose of study medication (PP) and had at least 1 post baseline observation on any efficacy parameter. Here 'n' signifies number of subjects analysed for this endpoint. |
| End point type         | Secondary  |
| End point timeframe:   | Baseline and Month 6 LOCF  |

| End point values                              | Group A1:<br>Subjects<br>Switched for<br>Efficacy Reason | Group A2:<br>Subjects<br>Switched for<br>Other Reason | Group B1:<br>Subjects<br>Switched from<br>Haloperidol<br>Decanoate | Group B2:<br>Subjects<br>Switched from<br>Flupentixol<br>Decanoate |
|---|--|---|--|--|
| Subject group type                            | Subject analysis set                                     | Subject analysis set                                  | Subject analysis set   | Subject analysis set   |
| Number of subjects analysed                   | 143  | 446   | 53   | 34   |
| Units: units on a scale                       |  |   |  |  |
| arithmetic mean (standard deviation)          |  |   |  |  |
| Baseline<br>(n=139,429,53,34,44,41,55,86,197) | 55.3 (± 12.31)   | 59 (± 13.62)  | 48.7 (± 12.53)   | 59.6 (± 11.2)  |
| Month 6<br>LOCF(n=139,429,53,34,44,41,55,197) | 5.5 (± 12.31)  | 8.8 (± 14.37)   | 5.2 (± 13)   | 6.1 (± 14.94)  |

| End point values                     | Group B3:<br>Subjects<br>Switched from<br>Fluphenazine<br>Decanoate | Group B4:<br>Subjects<br>Switched from<br>Zuclopentixol-<br>Decanoate | Group B5:<br>Subjects<br>Switched from<br>Risperidone<br>Micropsheres | Group C              |
|--------------------------------------|---|---|---|----------------------|
| Subject group type                   | Subject analysis set  | Subject analysis set  | Subject analysis set  | Subject analysis set |
| Number of subjects analysed          | 44  | 41  | 55  | 207                  |
| Units: units on a scale              |   |   |   |                      |
| arithmetic mean (standard deviation) |   |   |   |                      |

|   |                |                |                |                |
|---|----------------|----------------|----------------|----------------|
| Baseline<br>(n=139,429,53,34,44,41,55,86,197) | 53.5 (± 12.16) | 52.9 (± 15.63) | 60.1 (± 17.92) | 43.9 (± 14.99) |
| Month 6<br>LOCF(n=139,429,53,34,44,41,55,197) | 6 (± 11.58)    | 6.4 (± 15.21)  | 5.2 (± 15.31)  | 19 (± 18.67)   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Health Status (Self-Reported Health Status Questionnaire [SF-36]) at Month 6

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Health Status (Self-Reported Health Status Questionnaire [SF-36]) at Month 6 |
|-----------------|--|

End point description:

The SF-36 is a validated self-rated health status instrument used to assess subjects across several domains. The SF-36 consists of 8 multi-item scales: limitations in physical functioning due to health problems; limitations in usual role activities due to physical health problems; bodily pain; general health perception; vitality (energy and fatigue); limitations in social functioning due to physical or mental health problems; limitations in usual role activities due to personal or emotional problems; and general mental health (psychological distress and well-being). These scales are scored from 0 to 100, with higher scores indicating better health. The SF-36 was also scored as- Physical Component - Scale Score (PCS) and Mental Component - Scale Score (MCS). Higher scores indicated better health. Efficacy analysis included all subjects who received at least 1 dose of PP and had at least 1 post baseline observation on any efficacy parameter.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Month 6 LOCF

| End point values                                   | Group A1:<br>Subjects<br>Switched for<br>Efficacy Reason | Group A2:<br>Subjects<br>Switched for<br>Other Reason | Group B1:<br>Subjects<br>Switched from<br>Haloperidol<br>Decanoate | Group B2:<br>Subjects<br>Switched from<br>Flupentixol<br>Decanoate |
|--|--|---|--|--|
| Subject group type                                 | Subject analysis set                                     | Subject analysis set                                  | Subject analysis set   | Subject analysis set   |
| Number of subjects analysed                        | 143  | 446   | 53   | 34   |
| Units: units on a scale                            |  |   |  |  |
| arithmetic mean (standard deviation)               |  |   |  |  |
| Baseline-PCS<br>(n=130,399,46,33,42,38,49,182)     | 48 (± 9.47)  | 48.7 (± 8.76)   | 49.4 (± 7.48)  | 49.3 (± 9.71)  |
| Month 6 LOCF-PCS<br>(n=130,399,46,33,42,38,49,182) | 2.2 (± 7.7)  | 1.2 (± 8.22)  | 1.4 (± 6.5)  | 2.2 (± 7.43)   |
| Baseline-MCS<br>(n=130,399,46,33,42,38,49,182)     | 33.5 (± 12.43)   | 35.9 (± 12.65)  | 38.1 (± 12.5)  | 37.8 (± 15.39)   |
| Month 6 LOCF-MCS<br>(n=130,399,46,33,42,38,49,182) | 6.6 (± 10.67)  | 5.4 (± 12.8)  | 4.4 (± 13.22)  | 6.8 (± 15.19)  |

| End point values | Group B3:<br>Subjects<br>Switched from<br>Fluphenazine<br>Decanoate | Group B4:<br>Subjects<br>Switched from<br>Zuclopentixol-<br>Decanoate | Group B5:<br>Subjects<br>Switched from<br>Risperidone<br>Micropsheres | Group C |
|------------------|---|---|---|---------|
|                  |   |   |   |         |

| Subject group type                                 | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
|--|----------------------|----------------------|----------------------|----------------------|
| Number of subjects analysed                        | 44                   | 41                   | 55                   | 207                  |
| Units: units on a scale                            |                      |                      |                      |                      |
| arithmetic mean (standard deviation)               |                      |                      |                      |                      |
| Baseline-PCS<br>(n=130,399,46,33,42,38,49,182)     | 46.9 (± 9.59)        | 48.7 (± 9.7)         | 49.2 (± 9.72)        | 47.3 (± 9.5)         |
| Month 6 LOCF-PCS<br>(n=130,399,46,33,42,38,49,182) | 2.6 (± 10.27)        | 0 (± 7.69)           | 0.1 (± 8.21)         | 1.9 (± 8.96)         |
| Baseline-MCS<br>(n=130,399,46,33,42,38,49,182)     | 36.6 (± 13.41)       | 36.2 (± 12.7)        | 35.8 (± 16)          | 28.7 (± 12.93)       |
| Month 6 LOCF-MCS<br>(n=130,399,46,33,42,38,49,182) | 2.9 (± 13.96)        | 8.7 (± 12.17)        | 5.4 (± 13.52)        | 11 (± 15.19)         |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Measure of Health Outcome (EQ-5D) Visual Analog Scale (VAS) at Month 6

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Measure of Health Outcome (EQ-5D) Visual Analog Scale (VAS) at Month 6 |
|-----------------|--|

End point description:

The EQ-5D is designed for self-completion by subjects and consists of 2 scales - the EQ-5D descriptive system and the EQ visual analog scale (EQ VAS). The EQ-5D descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 3 levels: 1=no problems, 2=some problems, or 3=severe problems. The EQ VAS records the subjects self-rated health on a vertical, visual analog scale, with 0 representing the worst imaginable health state and 100 representing the best imaginable health state. The EQ VAS is used as a quantitative measure of health outcome as scored by the individual subject. Efficacy analysis included all subjects who received at least 1 dose of PP and had at least 1 post baseline observation on any efficacy parameter. Here 'n' signifies number of subjects analysed for this endpoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Month 6 LOCF

| End point values                              | Group A1:<br>Subjects<br>Switched for<br>Efficacy Reason | Group A2:<br>Subjects<br>Switched for<br>Other Reason | Group B1:<br>Subjects<br>Switched from<br>Haloperidol<br>Decanoate | Group B2:<br>Subjects<br>Switched from<br>Flupentixol<br>Decanoate |
|---|--|---|--|--|
| Subject group type                            | Subject analysis set                                     | Subject analysis set                                  | Subject analysis set   | Subject analysis set   |
| Number of subjects analysed                   | 143  | 446   | 53   | 34   |
| Units: units on a scale                       |  |   |  |  |
| arithmetic mean (standard deviation)          |  |   |  |  |
| Baseline<br>(n=132,398,46,33,43,38,49,179)    | 57.98 (± 21.179)   | 61.18 (± 19.987)                                      | 60.37 (± 20.93)  | 61.32 (± 21.574)   |
| Month 6<br>LOCF(n=132,398,46,33,43,38,49,179) | 8.94 (± 18.89)   | 8.09 (± 22.543)                                       | 8.1 (± 24.876)   | 15.32 (± 19.729)   |

| <b>End point values</b>                       | Group B3:<br>Subjects<br>Switched from<br>Fluphenazine<br>Decanoate | Group B4:<br>Subjects<br>Switched from<br>Zuclopentixol-<br>Decanoate | Group B5:<br>Subjects<br>Switched from<br>Risperidone<br>Microspheres | Group C              |
|---|---|---|---|----------------------|
| Subject group type                            | Subject analysis set  | Subject analysis set  | Subject analysis set  | Subject analysis set |
| Number of subjects analysed                   | 44  | 41  | 55  | 207                  |
| Units: units on a scale                       |   |   |   |                      |
| arithmetic mean (standard deviation)          |   |   |   |                      |
| Baseline<br>(n=132,398,46,33,43,38,49,179)    | 61.53 (±<br>22.105)   | 64.21 (±<br>18.805)   | 56.26 (±<br>28.171)   | 55.3 (±<br>22.608)   |
| Month 6<br>LOCF(n=132,398,46,33,43,38,49,179) | 4.95 (± 21.94)  | 7.3 (± 22.765)  | 9.31 (±<br>27.865)  | 12.15 (±<br>28.022)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Subject well-being (Subjective Well-Being under Neuroleptics Scale [SWN-S]) at Month 6

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Subject well-being (Subjective Well-Being under Neuroleptics Scale [SWN-S]) at Month 6 |
|-----------------|--|

End point description:

The SWN-S is an instrument to measure the subjective changes, such as restrictions in emotionality, the clarity of thinking, and spontaneity, that are often referred as 'pharmacogenic depression' or the 'neuroleptic induced deficit syndrome'. It consist of 20 items (10 positive items and 10 negative items). Each item of the SWN -S is rated on 6-point Likert scale (1=not at all, 2=hardly at all, 3=a little, 4=somewhat, 5=much, 6=very much). There are 5 sub scores (mental functioning, social integration, emotional regulation, physical functioning and self-control) and a SWN-S total score. After reversing the score of the 10 negative items, the item scores are added to generate the subscale scores and the total score. Efficacy analysis included all subjects who received at least 1 dose of PP and had at least 1 post baseline observation on any efficacy parameter. Here 'n' signifies number of subjects analysed for this endpoint.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline and Month 6 |           |

| <b>End point values</b>                       | Group A1:<br>Subjects<br>Switched for<br>Efficacy Reason | Group A2:<br>Subjects<br>Switched for<br>Other Reason | Group B1:<br>Subjects<br>Switched from<br>Haloperidol<br>Decanoate | Group B2:<br>Subjects<br>Switched from<br>Flupentixol<br>Decanoate |
|---|--|---|--|--|
| Subject group type                            | Subject analysis set                                     | Subject analysis set                                  | Subject analysis set   | Subject analysis set   |
| Number of subjects analysed                   | 143  | 446   | 53   | 34   |
| Units: units on a scale                       |  |   |  |  |
| arithmetic mean (standard deviation)          |  |   |  |  |
| Baseline<br>(n=129,392,46,33,43,37,47,180)    | 77.2 (± 17.97)   | 81 (± 16.9)   | 83.7 (± 12.48)   | 83.5 (± 18.64)   |
| Month 6<br>LOCF(n=129,392,46,33,43,37,47,180) | 6.6 (± 14.06)  | 5 (± 16.14)   | 3.2 (± 13.59)  | 8.3 (± 17.46)  |

| <b>End point values</b>                       | Group B3:<br>Subjects<br>Switched from<br>Fluphenazine<br>Decanoate | Group B4:<br>Subjects<br>Switched from<br>Zuclopentixol-<br>Decanoate | Group B5:<br>Subjects<br>Switched from<br>Risperidone<br>Micropsheres | Group C              |
|---|---|---|---|----------------------|
| Subject group type                            | Subject analysis set  | Subject analysis set  | Subject analysis set  | Subject analysis set |
| Number of subjects analysed                   | 44  | 41  | 55  | 207                  |
| Units: units on a scale                       |   |   |   |                      |
| arithmetic mean (standard deviation)          |   |   |   |                      |
| Baseline<br>(n=129,392,46,33,43,37,47,180)    | 81 (± 17.2)   | 83 (± 15.29)  | 80.8 (± 22.19)  | 73.8 (± 15.5)        |
| Month 6<br>LOCF(n=129,392,46,33,43,37,47,180) | 2.9 (± 15.5)  | 4.3 (± 14.84)   | 3.6 (± 15.65)   | 9.7 (± 20.57)        |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to Month 6

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 13.0 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Group A |
|-----------------------|---------|

Reporting group description:

Non-acute subjects switched from oral antipsychotics

|                       |         |
|-----------------------|---------|
| Reporting group title | Group C |
|-----------------------|---------|

Reporting group description:

Acute subjects switched from oral antipsychotics

|                       |         |
|-----------------------|---------|
| Reporting group title | Group B |
|-----------------------|---------|

Reporting group description:

Non-acute subjects switched from long acting antipsychotics

| <b>Serious adverse events</b>                                       | Group A           | Group C           | Group B           |
|---|-------------------|-------------------|-------------------|
| Total subjects affected by serious adverse events                   |                   |                   |                   |
| subjects affected / exposed   | 90 / 593 (15.18%) | 25 / 212 (11.79%) | 34 / 230 (14.78%) |
| number of deaths (all causes)                                       | 2                 | 2                 | 0                 |
| number of deaths resulting from adverse events                      |                   |                   |                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                   |                   |
| Lung Squamous Cell Carcinoma Stage Ii                               |                   |                   |                   |
| subjects affected / exposed   | 0 / 593 (0.00%)   | 1 / 212 (0.47%)   | 0 / 230 (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             |
| Vascular disorders  |                   |                   |                   |
| Arterial Stenosis Limb  |                   |                   |                   |
| subjects affected / exposed   | 1 / 593 (0.17%)   | 0 / 212 (0.00%)   | 0 / 230 (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             |
| Arteriosclerosis Obliterans   |                   |                   |                   |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                                 | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Deep Vein Thrombosis</b>                                 |                 |                 |                 |
| subjects affected / exposed                                 | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Hypertensive Crisis</b>                                  |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 593 (0.00%) | 1 / 212 (0.47%) | 0 / 230 (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           |
| <b>Surgical and medical procedures</b>                      |                 |                 |                 |
| <b>Cochlea Implant</b>                                      |                 |                 |                 |
| subjects affected / exposed                                 | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Pregnancy, puerperium and perinatal conditions</b>       |                 |                 |                 |
| <b>Abortion Spontaneous</b>                                 |                 |                 |                 |
| subjects affected / exposed                                 | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>General disorders and administration site conditions</b> |                 |                 |                 |
| <b>Irritability</b>   |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 593 (0.00%) | 1 / 212 (0.47%) | 0 / 230 (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           |
| <b>Social circumstances</b>                                 |                 |                 |                 |
| <b>Miscarriage of Partner</b>                               |                 |                 |                 |
| subjects affected / exposed                                 | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Respiratory, thoracic and mediastinal disorders</b>      |                 |                 |                 |
| <b>Acute Respiratory Failure</b>                            |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 593 (0.00%) | 1 / 212 (0.47%) | 0 / 230 (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           |
| <b>Aspiration</b>                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Chronic Obstructive Pulmonary Disease</b>    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Pulmonary Oedema</b>                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Psychiatric disorders</b>                    |                 |                 |                 |
| <b>Abnormal Behaviour</b>                       |                 |                 |                 |
| subjects affected / exposed                     | 2 / 593 (0.34%) | 0 / 212 (0.00%) | 0 / 230 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Acute Psychosis</b>                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 1 / 212 (0.47%) | 0 / 230 (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           |
| <b>Aggression</b>                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Alcohol Abuse</b>                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Agitation</b>                                |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 5 / 593 (0.84%) | 0 / 212 (0.00%) | 2 / 230 (0.87%) |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Anxiety</b>                                  |                 |                 |                 |
| subjects affected / exposed                     | 8 / 593 (1.35%) | 2 / 212 (0.94%) | 2 / 230 (0.87%) |
| occurrences causally related to treatment / all | 4 / 9           | 2 / 2           | 1 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Apathy</b>                                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Completed Suicide</b>                        |                 |                 |                 |
| subjects affected / exposed                     | 2 / 593 (0.34%) | 1 / 212 (0.47%) | 0 / 230 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 2           | 0 / 1           | 0 / 0           |
| <b>Catatonia</b>                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Delusion</b>                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Delusional Disorder, Unspecified Type</b>    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Depression</b>                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 1 / 212 (0.47%) | 0 / 230 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Drug Abuse</b>                               |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| Hallucination                                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hallucination, Visual                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| Hypochondriasis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Insomnia  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| Hypomania                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Intentional Self-Injury                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Obsessive-Compulsive Disorder                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Personality Disorder                            |                 |                 |                 |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 593 (0.00%)  | 0 / 212 (0.00%)  | 1 / 230 (0.43%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Psychiatric Decompensation</b>               |                  |                  |                  |
| subjects affected / exposed                     | 2 / 593 (0.34%)  | 0 / 212 (0.00%)  | 0 / 230 (0.00%)  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Psychotic Disorder</b>                       |                  |                  |                  |
| subjects affected / exposed                     | 21 / 593 (3.54%) | 12 / 212 (5.66%) | 12 / 230 (5.22%) |
| occurrences causally related to treatment / all | 9 / 25           | 5 / 13           | 10 / 12          |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Schizophrenia</b>                            |                  |                  |                  |
| subjects affected / exposed                     | 12 / 593 (2.02%) | 4 / 212 (1.89%)  | 6 / 230 (2.61%)  |
| occurrences causally related to treatment / all | 5 / 12           | 2 / 4            | 3 / 7            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Schizophrenia, Paranoid Type</b>             |                  |                  |                  |
| subjects affected / exposed                     | 4 / 593 (0.67%)  | 0 / 212 (0.00%)  | 1 / 230 (0.43%)  |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Social Avoidant Behaviour</b>                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 593 (0.17%)  | 0 / 212 (0.00%)  | 0 / 230 (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            |
| <b>Stress</b>                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 593 (0.17%)  | 0 / 212 (0.00%)  | 0 / 230 (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            |
| <b>Suicidal Ideation</b>                        |                  |                  |                  |
| subjects affected / exposed                     | 3 / 593 (0.51%)  | 1 / 212 (0.47%)  | 3 / 230 (1.30%)  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            | 1 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Suicide Attempt</b>                          |                  |                  |                  |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 3 / 593 (0.51%) | 2 / 212 (0.94%) | 0 / 230 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Tension   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| Thinking Abnormal                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| Injury, poisoning and procedural complications  |                 |                 |                 |
| Femoral Neck Fracture                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Animal Bite                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| Femur Fracture                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| 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                               |                 |                 |                 |
| Angina Pectoris                                 |                 |                 |                 |
| alternative assessment type: Systematic         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Acute Myocardial Infarction                     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 593 (0.00%) | 1 / 212 (0.47%) | 0 / 230 (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           |
| <b>Atrial Fibrillation</b>                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Sinus Tachycardia</b>                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Nervous system disorders</b>                 |                 |                 |                 |
| <b>Akathisia</b>                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Convulsion</b>                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Dyskinesia</b>                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Extrapyramidal Disorder</b>                  |                 |                 |                 |
| subjects affected / exposed                     | 2 / 593 (0.34%) | 0 / 212 (0.00%) | 0 / 230 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Hypertonia</b>                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 1 / 212 (0.47%) | 0 / 230 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Psychomotor Hyperactivity</b>                |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                            | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Gastrointestinal disorders</b>                      |                 |                 |                 |
| <b>Abdominal Pain Lower</b>                            |                 |                 |                 |
| subjects affected / exposed                            | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Abdominal Pain</b>                                  |                 |                 |                 |
| subjects affected / exposed                            | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Anal Prolapse</b>                                   |                 |                 |                 |
| subjects affected / exposed                            | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Enterocolitis Haemorrhagic</b>                      |                 |                 |                 |
| subjects affected / exposed                            | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Hepatobiliary disorders</b>                         |                 |                 |                 |
| <b>Cholangitis</b>                                     |                 |                 |                 |
| subjects affected / exposed                            | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Liver Disorder</b>                                  |                 |                 |                 |
| subjects affected / exposed                            | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| <b>Musculoskeletal and connective tissue disorders</b> |                 |                 |                 |
| <b>Arthritis</b>                                       |                 |                 |                 |
| subjects affected / exposed                            | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Back Pain                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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                     |                 |                 |                 |
| Bronchopneumonia                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Appendicitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| Influenza                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| Pyelonephritis                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 593 (0.17%) | 0 / 212 (0.00%) | 0 / 230 (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           |
| Metabolism and nutrition disorders              |                 |                 |                 |
| Hypoglycaemia                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 593 (0.00%) | 0 / 212 (0.00%) | 1 / 230 (0.43%) |
| 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 %

| <b>Non-serious adverse events</b>                     | Group A            | Group C           | Group B           |
|---|--------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events |                    |                   |                   |
| subjects affected / exposed                           | 162 / 593 (27.32%) | 65 / 212 (30.66%) | 48 / 230 (20.87%) |
| Nervous system disorders                              |                    |                   |                   |
| Headache  |                    |                   |                   |

|  |                          |                         |                        |
|--|--------------------------|-------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)   | 33 / 593 (5.56%)<br>36   | 13 / 212 (6.13%)<br>22  | 14 / 230 (6.09%)<br>22 |
| General disorders and administration<br>site conditions<br>Injection Site Pain<br>subjects affected / exposed<br>occurrences (all) | 73 / 593 (12.31%)<br>122 | 29 / 212 (13.68%)<br>49 | 14 / 230 (6.09%)<br>19 |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)  | 51 / 593 (8.60%)<br>58   | 23 / 212 (10.85%)<br>30 | 15 / 230 (6.52%)<br>15 |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)  | 34 / 593 (5.73%)<br>48   | 11 / 212 (5.19%)<br>19  | 10 / 230 (4.35%)<br>11 |
| Psychotic Disorder<br>subjects affected / exposed<br>occurrences (all)   | 16 / 593 (2.70%)<br>18   | 11 / 212 (5.19%)<br>12  | 7 / 230 (3.04%)<br>8   |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 07 May 2010     | Amendment INT-1 was implemented prior to first-subject/first-visit and included the following changes: Additional clarification of the inclusion criteria regarding the definition of acute and non-acute subjects and corrections of the recruitment instructions and dosing and switching instructions.  |
| 10 June 2010    | Amendment INT-2 was implemented prior to first-subject/first-visit and consisted of updates and corrections regarding the assessment scales included in the attachments.   |
| 29 October 2010 | Amendment INT-3 was implemented before any subject had started the optional extension phase and consisted of the following changes: 1) The duration of the optional extension phase was changed from a maximum of 12 months per subject to a maximum of 12 months after the last subject had completed the 6-month study period, or until PP became available in the respective country; 2) Additional text was added to clarify that IEQ would only be administered in a limited number of countries, depending on availability of the scale in local languages; 3) In some countries, it is standard practice that PANSS is assessed by other qualified personnel besides the investigator (e.g. nurses specialized in psychiatry with specific PANSS training). In order to allow this type of qualified personnel to rate the PANSS, the text was updated. |

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study limitations were the open-label and single-arm design.

Notes: