# Clinical trial results:
# A 26-week, International, Multicenter, Open-label Phase IIIb Study of the Safety and Tolerability of Quetiapine Fumarate (SEROQUEL) Immediate-release Tablets in Daily Doses of 400 mg to 800 mg in Children and Adolescents with Bipolar I Disorder and Adolescents with Schizophrenia

## Summary

| | |
|---|---|
| EudraCT number | 2004-000751-42 |
| Trial protocol | DE |
| Global end of trial date | 10 July 2008 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 01 February 2017 |
| First version publication date | 06 August 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | D1441C00150 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00227305 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | AstraZeneca |
| Sponsor organisation address | 1 MedImmune Way, Gaithersburg, United States, 20878 |
| Public contact | Heather Wray, Seroquel Medical Science Director, MD, AstraZeneca, 46 0 31 706 4082, AZTrial_Results_Posting@astrazeneca.com |
| Scientific contact | Heather Wray, Seroquel Medical Science Director, MD, AstraZeneca, 46 0 31 706 4082, AZTrial_Results_Posting@astrazeneca.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-000324-PIP01-08 |
| 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:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 10 July 2008 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 July 2008 |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 July 2008 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to assess the safety and tolerability of quetiapine in children and adolescent patients with bipolar I disorder and in adolescents with schizophrenia by: 1) the incidence and nature of overall AEs; 2) the rate of patient withdrawal due to AEs; 3) the changes from the open-label baseline to Week 26 in clinical laboratory results, vital signs, weight, body mass index, ECG and physical exam findings; 4) the changes from open-labe baseline to Week 26 in the Simpson-Angus Scale total score, the Barnes Akathisia Scale global score and the Abnormal Involuntary Movement Scale total score.

Protection of trial subjects:

The final study protocol, including the final version of the Informed Consent Form was approved or given a favorable opinion in writing by an Institutional Review Board or Independent Ethics Committee as appropriate. The principal investigator was responsible for informing the IRB or IEC of any amendment to the protocol and re-approved in accorndance with local requirements. Progress reports and notifications of serious adverse drug reactions were provided to the IRB or IEC according to local regulations and guidelines.

The study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Conference on Harmonization (ICH)/ Good Clinical Practice (GCP) and applicable regulatory requirements and the AstraZeneca policy on Bioethics.

The principal investigator at each center ensured that both the patient (assent) and the parent or legal guardian (consent) were given full and adequate oral and written information about the nature, purpose, and possible risks and benefits of the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 26 August 2004 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 248 |
| Country: Number of subjects enrolled | Puerto Rico: 4 |
| Country: Number of subjects enrolled | Poland: 7 |
| Country: Number of subjects enrolled | Russian Federation: 34 |
| Country: Number of subjects enrolled | Serbia: 20 |
| Country: Number of subjects enrolled | Ukraine: 20 |

| | |
|---|---|
| Country: Number of subjects enrolled | India: 5 |
| Country: Number of subjects enrolled | Malaysia: 6 |
| Country: Number of subjects enrolled | Philippines: 30 |
| Country: Number of subjects enrolled | South Africa: 6 |
| Worldwide total number of subjects | 380 |
| EEA total number of subjects | 7 |

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) | 46 |
| Adolescents (12-17 years) | 323 |
| Adults (18-64 years) | 11 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Enrollment was contingent on completing one of 2 short term efficacy studies, recruitment period August 2004 through July 2007 at 59 international clinical research sites

### Pre-assignment

Screening details:

Required to have completed one feeder study, either bipolar mania study D1441C00149 or schizophrenia study D1441C00112 and be willing to participate in a 26 week open label study and be between the ages of 10 and 18 years at the time of consent for this study, initial titration to maintain blind in feeder study

### 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** | Quetiapine |

Arm description:

Quetiapine 400mg/day to 800mg/day

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | quetiapine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Titrated from single 50 mg dose to target dose of 400-800 mg/day

| **Number of subjects in period 1** | Quetiapine |
|---|---|
| Started | 380 |
| Drug received | 380 |
| Completed | 237 |
| Not completed | 143 |
| LEAVING TOWN FOR 6 WEEKS | 1 |
| Consent withdrawn by subject | 42 |
| Physician decision | 3 |
| Adverse event, non-fatal | 40 |
| PERIOD SHORTENED FROM 6 wks to 4 wks | 1 |
| MOVED OUT OF AREA | 3 |
| Lost to follow-up | 33 |
| Study specific discontinuation | 12 |

| | |
|---|---|
| NECESSITY OF USING ANTI DEPRESSANT | 1 |
| Lack of efficacy | 7 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Quetiapine |
| Reporting group description: | |
| Quetiapine 400mg/day to 800mg/day | |

| Reporting group values | Quetiapine | Total | |
|---|---|---|---|
| Number of subjects | 380 | 380 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 46 | 46 | |
| Adolescents (12-17 years) | 323 | 323 | |
| Adults (18-64 years) | 11 | 11 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 14.4 | | |
| standard deviation | ± 2.2 | - | |
| Gender, Male/Female<br>Units: Participants | | | |
| Female | 154 | 154 | |
| Male | 226 | 226 | |
| Age, Customized<br>Units: Subjects | | | |
| 10 - 12 years | 87 | 87 | |
| 13 - 18 years | 293 | 293 | |
| Study Specific Characteristic<br>Units: Subjects | | | |
| Bipolar | 205 | 205 | |
| Schizophrenia | 175 | 175 | |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | Safety Analysis Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All subjects who received at least one dose of experimental drug | |

| **Reporting group values** | Safety Analysis Set | | |
|---|---|---|---|
| Number of subjects | 380 | | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 46 | | |
| Adolescents (12-17 years) | 323 | | |
| Adults (18-64 years) | 11 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 14.4 | | |
| standard deviation | ± 2.2 | | |
| Gender, Male/Female<br>Units: Participants | | | |
| Female | 154 | | |
| Male | 226 | | |
| Age, Customized<br>Units: Subjects | | | |
| 10 - 12 years | 87 | | |
| 13 - 18 years | 293 | | |
| Study Specific Characteristic<br>Units: Subjects | | | |
| Bipolar | 205 | | |
| Schizophrenia | 175 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Quetiapine |
| Reporting group description: | |
| Quetiapine 400mg/day to 800mg/day | |
| Subject analysis set title | Safety Analysis Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All subjects who received at least one dose of experimental drug | |

### Primary: Incidence and nature of adverse events (AEs)

| | |
|---|---|
| End point title | Incidence and nature of adverse events (AEs)[1] |
| End point description: | |
| Number of participants that had AE which occurred from first dose date to last dose date + 30 days. | |
| End point type | Primary |
| End point timeframe: | |
| from open label to week 26+ 30 days | |

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 employed only, no statistical comparisons were employed in this safety extension study

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 380 | | | |
| Units: Participants | 321 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of patients withdrawn due to AEs.

| | |
|---|---|
| End point title | Number of patients withdrawn due to AEs.[2] |
| End point description: | |
| Number of subjects who withdrew from the study due to AEs. | |
| End point type | Primary |
| End point timeframe: | |
| during 26 weeks of treatment | |

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 employed only, no statistical comparisons were employed in this safety extension study

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 380 | | | |
| Units: Participants | 37 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Changes in laboratory test results (Prolactin)

| End point title | Changes in laboratory test results (Prolactin)[3] |
|---|---|

End point description:

Clinical important shift to high prolactin from open-label (OL) baseline to week 26. High Prolactin is defined as value >26 ug/L for female and value >20 ug/L for male.

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

End point timeframe:

Duration of study participation

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 employed only, no statistical comparisons were employed in this safety extension study

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 380 | | | |
| Units: Participants | 19 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Categorical Change from OL baseline to week 26 in Simpson-Angus Scale (SAS)total score

| End point title | Categorical Change from OL baseline to week 26 in Simpson-Angus Scale (SAS)total score[4] |
|---|---|

End point description:

Number of patients for who the total score is estimated as worse. The Simpson Angus Scale (SAS)is used to assess Parkinsonian symptoms (a type of movement disorders). The score was calculated as the sum of the 10 individual item scores. Total Score ranges from 0-40 (normal to worse). Individual item scale range from 0 to 4 (normal to worse). Improved define as those with a <= -1 change in SAS total score. Worsened defined as those with a >=1 change in SAS total score.

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

End point timeframe:

OL baseline to week 26

Notes:

[4] - 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 employed only, no statistical comparisons were employed in this safety extension study

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 373 | | | |
| Units: Participants | 34 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Categorical Change from baseline in Barnes Akathisia Rating Scale (BARS) global score

| End point title | Categorical Change from baseline in Barnes Akathisia Rating Scale (BARS) global score[5] |
|---|---|

End point description:

Number of patients for who the total score is estimated as worse. The Barnes Akathisia Rating Scale (BARS) global score is used to measure Akathisia (a type of movement disorders). BARS is the item 4 score from the BARS assessment. The scale is from a range 0-5 (normal to worse). Change from baseline in BARS global score increase means worse. Improved defined as those with a <= -1 change in BARS global score. Worsened defined as those with a >= 1 change in BARS global score.

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

End point timeframe:

26 weeks of treatment

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 employed only, no statistical comparisons were employed in this safety extension study

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 373 | | | |
| Units: Participants | 11 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Change from baseline in weight

| End point title | Change from baseline in weight[6] |
|---|---|

End point description:

Number with 7% or more increase (without adjustment for normal growth)

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

End point timeframe:

26 weeks of treatment

Notes:

[6] - 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 employed only, no statistical comparisons were employed in this safety extension study

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 373 | | | |
| Units: Participants | 134 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Change from baseline in supine pulse

| End point title | Change from baseline in supine pulse[7] |
|---|---|

End point description:

Change from OL baseline to week 26 in supine pulse (bpm)

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

End point timeframe:

OL baseline to week 26

Notes:

[7] - 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 employed only, no statistical comparisons were employed in this safety extension study

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 375 | | | |
| Units: bpm | | | | |
| arithmetic mean (standard deviation) | 0.8 (± 14.75) | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Change from OL baseline in supine systolic BP.

| End point title | Change from OL baseline in supine systolic BP.[8] |
|---|---|

End point description:

Changes from OL baseline to the final visits in Supine systolic BP (mmHg)

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

End point timeframe:

OL baseline to Week 26

Notes:

[8] - 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 employed only, no statistical comparisons were employed in this safety extension study

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 375 | | | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | 1.7 (± 11.52) | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Change from OL baseline in supine diastolic BP.

| End point title | Change from OL baseline in supine diastolic BP.[9] |
|---|---|

End point description:

Changes from OL baseline to the final visits in Supine diastolic BP (mmHg)

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

End point timeframe:

OL baseline to Week 26

Notes:

[9] - 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 employed only, no statistical comparisons were employed in this safety extension study

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 375 | | | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | 1.3 (± 9.22) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in Children's Global Assessment Scale (CGAS) score

| End point title | Change from baseline in Children's Global Assessment Scale (CGAS) score |
|---|---|

End point description:

Children's Global Assessment Scale (CGAS) is used to rate the general functioning of children under the age of 18. It is the 100-point single-item score that was collected in the Clinical Report Form (CRF), scored from 0-100 (worse to normal).

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

End point timeframe:

OL Baseline to Week 26

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 320 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | 7 (± 13.9) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Changes in Tanner stage

| End point title | Changes in Tanner stage |
|---|---|

End point description:

Category shift in Tanner stage. Number of subjects who experienced the change is presented. Tanner stages (I-V) was used to characterize physical development in children, adolescents, and adults. The stages was based on external primary and secondary sex characteristics, such as the size of the breasts, genitalia, and development of pubic hair. Tanner stage is considered going up when the organs grow bigger.

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

End point timeframe:

Change from OL baseline to week 26 in the Tanner stage

| End point values | Quetiapine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 373 | | | |
| Units: Participants | 70 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Other AE module includes adverse events which occurred before first dose date to last dose date + 30 days.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 10.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Quetiapine |

Reporting group description:

Quetiapine 400mg/day to 800mg/day

| Serious adverse events | Quetiapine | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 46 / 380 (12.11%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Drug Toxicity | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Overdose | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 2 / 380 (0.53%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypertensive Crisis | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| Physical Assault | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac disorders | | | | |
| Myocarditis Post Infection | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nervous system disorders | | | | |
| Syncope | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General disorders and administration site conditions | | | | |
| Irritability | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood and lymphatic system disorders | | | | |
| Neutropenia | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Constipation | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary Hypertension | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Abnormal Behaviour | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aggression | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 4 / 380 (1.05%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Agitation | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bipola Disorder | | | |
| alternative dictionary used: MedDRA 10.0 | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 12 / 380 (3.16%) | | | |
| occurrences causally related to treatment / all | 2 / 13 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Delusion | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Disinhibition | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hostility | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hallucitnation Auditory | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mania | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Perceptual Alteration Paroxysmal | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|---|---|---|---|---|
| Pyschotic Disorder | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 2 / 380 (0.53%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Restlessness | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Schizophrenia | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 8 / 380 (2.11%) | | | |
| occurrences causally related to treatment / all | 1 / 11 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Schizophrenia, Paraniod Type | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Suicide Attempt | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infections and infestations | | | | |
| Amoebiasis | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Appendicitis | | | | |
| alternative dictionary used: MedDRA 10.0 | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 380 (0.53%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bacterial Infection | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cellulitis Staphylococcal | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Staphylococcal Infection | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper Respiratory Tract Infection | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Typhoid Fever | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary Tract Infection | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Metabolism and nutrition disorders | | | |
| Decreased Appetite | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycaemia | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 1 / 380 (0.26%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Quetiapine | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 340 / 380 (89.47%) | | |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 25 / 380 (6.58%) | | |
| occurrences (all) | 31 | | |
| Nervous system disorders | | | |
| DIZZINESS | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 26 / 380 (6.84%) | | |
| occurrences (all) | 38 | | |
| HEADACHE | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 43 / 380 (11.32%) | | |
| occurrences (all) | 102 | | |
| SOMNOLENCE | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 115 / 380 (30.26%) | | |
| occurrences (all) | 140 | | |

| | | | |
|---|---|---|---|
| SEDATION | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 72 / 380 (18.95%) | | |
| occurrences (all) | 80 | | |
| Gastrointestinal disorders | | | |
| DRY MOUTH | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 35 / 380 (9.21%) | | |
| occurrences (all) | 35 | | |
| FATIGUE | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 20 / 380 (5.26%) | | |
| occurrences (all) | 23 | | |
| NAUSEA | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 39 / 380 (10.26%) | | |
| occurrences (all) | 48 | | |
| VOMITING | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 43 / 380 (11.32%) | | |
| occurrences (all) | 53 | | |
| WEIGHT INCREASED | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 65 / 380 (17.11%) | | |
| occurrences (all) | 66 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| NASAL CONGESTION | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 20 / 380 (5.26%) | | |
| occurrences (all) | 21 | | |
| Psychiatric disorders | | | |
| AGITATION | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 26 / 380 (6.84%) | | |
| occurrences (all) | 37 | | |
| INSOMNIA | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 43 / 380 (11.32%) | | |
| occurrences (all) | 52 | | |
| IRRITABILITY | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 23 / 380 (6.05%) | | |
| occurrences (all) | 29 | | |
| Infections and infestations | | | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 27 / 380 (7.11%) | | |
| occurrences (all) | 29 | | |
| Metabolism and nutrition disorders | | | |
| INCREASED APPETITE | | | |
| alternative dictionary used: MedDRA 10.0 | | | |
| subjects affected / exposed | 76 / 380 (20.00%) | | |
| occurrences (all) | 78 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 04 December 2006 | Addition of CDRS-R Assessment to monitor for signs of emergent depression and to evaluate suicidal ideation |

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.

| |
|---|
| No comparator group, open label treatment, duration only 26 weeks - not long enough to assess full impact on growth and development |

Notes: