



## Clinical trial results:

### An open label study to evaluate the efficacy, safety and tolerability of RWJ333369 as adjunctive therapy in subjects with partial onset seizure

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

## Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2007-001801-99  |
| Trial protocol           | HU              |
| Global end of trial date | 05 October 2010 |

## Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 02 June 2016   |
| First version publication date | 02 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 | 333369EPY3004 |
|-----------------------|---------------|

### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00991757 |
| WHO universal trial number (UTN)   | -           |

Notes:

## Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Janssen-Cilag International N.V.  |
| Sponsor organisation address | Antwerpseweg 15-17, B-2340 Beerse, Belgium,   |
| Public contact               | Clinical Registry Group, Clinical Registry Group, +31 71 524 21 66,, ClinicalTrialsEU@its.jnj.com               |
| Scientific contact           | Janssen-Cilag International NV, Janssen-Cilag International NV, +31 71 524 21 66,, 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                       | 05 October 2010 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 05 October 2010 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this open label study is to determine the long-term safety and tolerability of RWJ-333369 as adjunctive treatment of partial onset seizures. Safety evaluation will include worsening of seizures, including rates of status epilepticus.

Protection of trial subjects:

Safety was evaluated by examining the incidence and severity of adverse events; laboratory safety (hematology, serum chemistry, serum lipid profile and urinalysis); Electrocardiogram, vital signs; physical and neurological examination.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 12 February 2007 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Argentina: 38          |
| Country: Number of subjects enrolled | Australia: 16          |
| Country: Number of subjects enrolled | Bulgaria: 33           |
| Country: Number of subjects enrolled | Canada: 19             |
| Country: Number of subjects enrolled | China: 110             |
| Country: Number of subjects enrolled | Croatia: 10            |
| Country: Number of subjects enrolled | Czech Republic: 33     |
| Country: Number of subjects enrolled | Finland: 17            |
| Country: Number of subjects enrolled | Germany: 19            |
| Country: Number of subjects enrolled | Hong Kong: 13          |
| Country: Number of subjects enrolled | Hungary: 25            |
| Country: Number of subjects enrolled | India: 137             |
| Country: Number of subjects enrolled | Malaysia: 9            |
| Country: Number of subjects enrolled | Norway: 11             |
| Country: Number of subjects enrolled | Poland: 62             |
| Country: Number of subjects enrolled | Korea, Republic of: 62 |
| Country: Number of subjects enrolled | Russian Federation: 99 |
| Country: Number of subjects enrolled | Sweden: 13             |
| Country: Number of subjects enrolled | Taiwan: 48             |

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Thailand: 37       |
| Country: Number of subjects enrolled | Ukraine: 81        |
| Country: Number of subjects enrolled | United States: 118 |
| Worldwide total number of subjects   | 1010               |
| EEA total number of subjects         | 223                |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 41  |
| Adults (18-64 years)                      | 952 |
| From 65 to 84 years                       | 17  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The study was initiated on 12 February 2007 and completed on 5 October 2010 involving subjects from 168 centers in 22 countries.

### Pre-assignment

Screening details:

Total 1010 subjects entered the study out of these 445 subjects completed the study while 565 subjects withdraw from the 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

|                              |                                  |
|------------------------------|----------------------------------|
| Are arms mutually exclusive? | Yes                              |
| <b>Arm title</b>             | Carsibamate less than (<) 400 mg |

Arm description:

Carsibamate (CRS) tablet modal dose less than 400 mg given orally per day

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Carsibamate  |
| Investigational medicinal product code |              |
| Other name                             | RWJ-333369   |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Carsibamate (CRS) tablet modal dose less than 400 mg given orally per day

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | Carisbamate 400-<600mg |
|------------------|------------------------|

Arm description:

Subjects received Carsibamate modal dose from 400 to less than 600 mg given orally per Day.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Carsibamate  |
| Investigational medicinal product code |              |
| Other name                             | RWJ-333369   |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Subjects received Carsibamate modal dose from 400 to less than 600 mg given orally per Day.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Carisbamate 600-800mg |
|------------------|-----------------------|

Arm description:

Subjects received Carsibamate modal dose from 600 to 800 mg given orally per Day.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Carsibamate  |
| Investigational medicinal product code |              |
| Other name                             | RWJ-333369   |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Subjects received Carsibamate modal dose from 600 to 800 mg given orally per Day.

|   |                         |
|---|-------------------------|
| <b>Arm title</b>  | Carsibamate >800-1000mg |
| Arm description:  |                         |
| Subjects received Carsibamate modal dose more than 800 to 1000 mg given orally per Day. |                         |
| Arm type  | Experimental            |
| Investigational medicinal product name  | Carsibamate             |
| Investigational medicinal product code  |                         |
| Other name  | RWJ-333369              |
| Pharmaceutical forms  | Tablet                  |
| Routes of administration  | Oral use                |

Dosage and administration details:

Subjects received Carsibamate modal dose more than 800 to 1000 mg given orally per Day.

| <b>Number of subjects in period 1</b> | Carsibamate less than (<) 400 mg | Carisbamate 400- <600mg | Carisbamate 600- 800mg |
|---------------------------------------|----------------------------------|-------------------------|------------------------|
| Started                               | 37                               | 521                     | 450                    |
| Completed                             | 10                               | 208                     | 225                    |
| Not completed                         | 27                               | 313                     | 225                    |
| Adverse event, serious fatal          | -                                | 2                       | 5                      |
| Consent withdrawn by subject          | 11                               | 152                     | 89                     |
| Adverse event, non-fatal              | 6                                | 49                      | 16                     |
| Other                                 | 10                               | 70                      | 86                     |
| Pregnancy                             | -                                | 6                       | 1                      |
| Lost to follow-up                     | -                                | 29                      | 21                     |
| Protocol deviation                    | -                                | 5                       | 7                      |

| <b>Number of subjects in period 1</b> | Carsibamate >800- 1000mg |
|---------------------------------------|--------------------------|
| Started                               | 2                        |
| Completed                             | 2                        |
| Not completed                         | 0                        |
| Adverse event, serious fatal          | -                        |
| Consent withdrawn by subject          | -                        |
| Adverse event, non-fatal              | -                        |
| Other                                 | -                        |
| Pregnancy                             | -                        |
| Lost to follow-up                     | -                        |
| Protocol deviation                    | -                        |



## Baseline characteristics

### Reporting groups

|   |                                  |
|---|----------------------------------|
| Reporting group title   | Carsibamate less than (<) 400 mg |
| Reporting group description:<br>Carsibamate (CRS) tablet modal dose less than 400 mg given orally per day                   |                                  |
| Reporting group title   | Carisbamate 400-<600mg           |
| Reporting group description:<br>Subjects received Carsibamate modal dose from 400 to less than 600 mg given orally per Day. |                                  |
| Reporting group title   | Carisbamate 600-800mg            |
| Reporting group description:<br>Subjects received Carsibamate modal dose from 600 to 800 mg given orally per Day.           |                                  |
| Reporting group title   | Carsibamate >800-1000mg          |
| Reporting group description:<br>Subjects received Carsibamate modal dose more than 800 to 1000 mg given orally per Day.     |                                  |

| Reporting group values                      | Carsibamate less than (<) 400 mg | Carisbamate 400-<600mg | Carisbamate 600-800mg |
|---|----------------------------------|------------------------|-----------------------|
| Number of subjects                          | 37                               | 521                    | 450                   |
| Title for AgeCategorical<br>Units: subjects |                                  |                        |                       |
| Children (2-11 years)                       | 0                                | 0                      | 0                     |
| Adolescents (12-17 years)                   | 3                                | 17                     | 21                    |
| Adults (18-64 years)                        | 34                               | 495                    | 421                   |
| From 65 to 84 years                         | 0                                | 9                      | 8                     |
| 85 years and over                           | 0                                | 0                      | 0                     |
| Title for AgeContinuous<br>Units: years     |                                  |                        |                       |
| arithmetic mean                             | 37.7                             | 35.4                   | 35.5                  |
| standard deviation                          | ± 11.84                          | ± 12.74                | ± 12.9                |
| Title for Gender<br>Units: subjects         |                                  |                        |                       |
| Female                                      | 23                               | 276                    | 210                   |
| Male  | 14                               | 245                    | 240                   |

| Reporting group values                      | Carsibamate >800-1000mg | Total |  |
|---|-------------------------|-------|--|
| Number of subjects                          | 2                       | 1010  |  |
| Title for AgeCategorical<br>Units: subjects |                         |       |  |
| Children (2-11 years)                       | 0                       | 0     |  |
| Adolescents (12-17 years)                   | 0                       | 41    |  |
| Adults (18-64 years)                        | 2                       | 952   |  |
| From 65 to 84 years                         | 0                       | 17    |  |
| 85 years and over                           | 0                       | 0     |  |
| Title for AgeContinuous<br>Units: years     |                         |       |  |
| arithmetic mean                             | 27                      | -     |  |
| standard deviation                          | ± 4.24                  | -     |  |

|                  |   |     |  |
|------------------|---|-----|--|
| Title for Gender |   |     |  |
| Units: subjects  |   |     |  |
| Female           | 1 | 510 |  |
| Male             | 1 | 500 |  |



## End points

### End points reporting groups

|   |                                  |
|---|----------------------------------|
| Reporting group title   | Carsibamate less than (<) 400 mg |
| Reporting group description:<br>Carsibamate (CRS) tablet modal dose less than 400 mg given orally per day   |                                  |
| Reporting group title   | Carisbamate 400-<600mg           |
| Reporting group description:<br>Subjects received Carsibamate modal dose from 400 to less than 600 mg given orally per Day.   |                                  |
| Reporting group title   | Carisbamate 600-800mg            |
| Reporting group description:<br>Subjects received Carsibamate modal dose from 600 to 800 mg given orally per Day.   |                                  |
| Reporting group title   | Carsibamate >800-1000mg          |
| Reporting group description:<br>Subjects received Carsibamate modal dose more than 800 to 1000 mg given orally per Day.   |                                  |
| Subject analysis set title  | Intent-to-treat (ITT) population |
| Subject analysis set type   | Intention-to-treat               |
| Subject analysis set description:<br>The intent-to treat (ITT) analyses set was defined as subjects who provided seizure diary data for at least 1 visit in the open-label extension. |                                  |

### Primary: Percentage of Subjects who were Responders

|   |   |
|---|---|
| End point title   | Percentage of Subjects who were Responders <sup>[1]</sup> |
| End point description:<br>Responders were defined as subjects who had at least a 50% reduction from baseline in monthly seizure rate. |   |
| End point type  | Primary   |
| End point timeframe:<br>Baseline up to End of Treatment   |   |

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

| End point values              | Intent-to-treat (ITT) population |  |  |  |
|-------------------------------|----------------------------------|--|--|--|
| Subject group type            | Subject analysis set             |  |  |  |
| Number of subjects analysed   | 1008 <sup>[2]</sup>              |  |  |  |
| Units: Percentage of Subjects |                                  |  |  |  |
| number (not applicable)       | 44.5                             |  |  |  |

Notes:

[2] - ITT Population

### Statistical analyses

No statistical analyses for this end point

### Primary: Percent Reduction from Baseline to Open-Label Phase in Partial Onset Seizure Frequency

|                 |   |
|-----------------|---|
| End point title | Percent Reduction from Baseline to Open-Label Phase in Partial Onset Seizure Frequency <sup>[3]</sup> |
|-----------------|---|

End point description:

Change in Partial Onset Seizure Frequency evaluated as the percent reduction from the pretreatment baseline phase in Partial Onset Seizure Frequency compared with the :Open-Label Extension phase

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

End point timeframe:

Baseline up to End of Treatment

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

| End point values              | Intent-to-treat (ITT) population |  |  |  |
|-------------------------------|----------------------------------|--|--|--|
| Subject group type            | Subject analysis set             |  |  |  |
| Number of subjects analysed   | 1008 <sup>[4]</sup>              |  |  |  |
| Units: Percent change         |                                  |  |  |  |
| median (full range (min-max)) | 43.48 (-398.1 to 100)            |  |  |  |

Notes:

[4] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Primary: Percent Reduction From Baseline to the Last 6 Months of the Open-Label Phase in Partial Onset Seizure Frequency

|                 |  |
|-----------------|--|
| End point title | Percent Reduction From Baseline to the Last 6 Months of the Open-Label Phase in Partial Onset Seizure Frequency <sup>[5]</sup> |
|-----------------|--|

End point description:

Change in Partial Onset Seizure Frequency evaluated as the percent reduction from the pretreatment baseline phase in Partial Onset Seizure Frequency compared with the :Open-Label Extension phase

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

End point timeframe:

Baseline upto 6 Months

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

| End point values              | Intent-to-treat (ITT) population |  |  |  |
|-------------------------------|----------------------------------|--|--|--|
| Subject group type            | Subject analysis set             |  |  |  |
| Number of subjects analysed   | 1008 <sup>[6]</sup>              |  |  |  |
| Units: Percent Change         |                                  |  |  |  |
| median (full range (min-max)) | 49.15 (-748.3 to 100)            |  |  |  |

Notes:

[6] - ITT Population

## Statistical analyses

No statistical analyses for this end point

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**Primary: Percentage of Subjects who are seizure free from Baseline to Open-Label Phase**

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|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects who are seizure free from Baseline to Open-Label Phase <sup>[7]</sup> |
|-----------------|--|

End point description:

Seizure-free days evaluated as the percent change from the pretreatment baseline phase in average monthly seizure-free days per 28 days compared with the Open-Label Phase phase.

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

End point timeframe:

Baseline upto End of treatment

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 were done, no inferential statistical analyses were performed

| End point values              | Intent-to-treat (ITT) population |  |  |  |
|-------------------------------|----------------------------------|--|--|--|
| Subject group type            | Subject analysis set             |  |  |  |
| Number of subjects analysed   | 962 <sup>[8]</sup>               |  |  |  |
| Units: Percentage of Subjects |                                  |  |  |  |
| number (not applicable)       | 5.8                              |  |  |  |

Notes:

[8] - ITT Population

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline upto End of treatment

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 12.1 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Carsibamate <400 mg |
|-----------------------|---------------------|

Reporting group description:

Carsibamate (CRS) tablet less than 400 mg given orally per day

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Carsibamate 400-<600mg |
|-----------------------|------------------------|

Reporting group description:

Carsibamate tablet 400 mg to less than 600 mg given orally per day

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Carisbamate 600-800 mg |
|-----------------------|------------------------|

Reporting group description:

Carsibamate tablet 600 mg to 800 mg given orally per day

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Carsibamate >800-1000mg |
|-----------------------|-------------------------|

Reporting group description:

Carsibamate tablet greater than 800 mg to 1000 mg given orally per day

| Serious adverse events  | Carsibamate <400 mg | Carsibamate 400-<600mg | Carisbamate 600-800 mg |
|---|---------------------|------------------------|------------------------|
| Total subjects affected by serious adverse events                   |                     |                        |                        |
| subjects affected / exposed   | 6 / 37 (16.22%)     | 74 / 521 (14.20%)      | 70 / 450 (15.56%)      |
| number of deaths (all causes)                                       | 0                   | 0                      | 0                      |
| number of deaths resulting from adverse events                      |                     |                        |                        |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                     |                        |                        |
| Adenocarcinoma  |                     |                        |                        |
| subjects affected / exposed   | 0 / 37 (0.00%)      | 1 / 521 (0.19%)        | 0 / 450 (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                  |
| Basal Cell Carcinoma  |                     |                        |                        |
| subjects affected / exposed   | 1 / 37 (2.70%)      | 0 / 521 (0.00%)        | 0 / 450 (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                  |
| Breast Cancer   |                     |                        |                        |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 2 / 521 (0.38%) | 0 / 450 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Fibroadenoma of Breast                          |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Lip And/Or Oral Cavity Cancer                   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Melanocytic Naevus                              |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Non-Hodgkin's Lymphoma                          |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Oligodendroglioma                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Thyroid Cancer                                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Uterine Leiomyoma                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Vascular disorders                              |                |                 |                 |
| Aneurysm Arteriovenous                          |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Hypotension                                     |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Surgical and medical procedures                 |                |                 |                 |
| Arthrodesis                                     |                |                 |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (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           |
| Cardiac Pacemaker Insertion                     |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Cataract Operation                              |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Elective Surgery                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Endocervical Curettage                          |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Hospitalisation                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Hysterectomy                                    |                |                 |                 |

|  |                |                 |                 |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed                          | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 3 / 450 (0.67%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 3           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0           |
| Medical Device Removal                               |                |                 |                 |
| subjects affected / exposed                          | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0           |
| Nasal Operation                                      |                |                 |                 |
| subjects affected / exposed                          | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Neurosurgery   |                |                 |                 |
| subjects affected / exposed                          | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0           |
| Ovarian Cystectomy                                   |                |                 |                 |
| subjects affected / exposed                          | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Spinal Fusion Surgery                                |                |                 |                 |
| subjects affected / exposed                          | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0           |
| Surgery  |                |                 |                 |
| subjects affected / exposed                          | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0           |
| Vagal Nerve Stimulator Removal                       |                |                 |                 |
| subjects affected / exposed                          | 0 / 37 (0.00%) | 2 / 521 (0.38%) | 0 / 450 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0           |
| General disorders and administration site conditions |                |                 |                 |
| Chest Pain   |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Drowning  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Pyrexia   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Reproductive system and breast disorders        |                |                 |                 |
| Benign Prostatic Hyperplasia                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Metrorrhagia                                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 2 / 521 (0.38%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Ovarian Cyst                                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                |                 |                 |
| Asphyxia  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Pneumonia Aspiration                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |



|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| Respiratory Distress                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Psychiatric disorders                           |                |                 |                 |
| Abnormal Behaviour                              |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Acute Psychosis                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Aggression                                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Agitation                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Anxiety   |                |                 |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (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           |
| Conversion Disorder                             |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Delirium  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Depression                                      |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 2 / 521 (0.38%) | 0 / 450 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Dysphoria                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Hallucination                                   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Hypomania                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Major Depression                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Psychotic Disorder                              |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 2 / 521 (0.38%) | 0 / 450 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Suicide Attempt                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 3 / 521 (0.58%) | 0 / 450 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 4           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Investigations                                  |                |                 |                 |
| Diagnostic Procedure                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Electroencephalogram                            |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Liver Function Test Abnormal                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Injury, poisoning and procedural complications  |                |                 |                 |
| Accidental Exposure                             |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Ankle Fracture                                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Brain Contusion                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Cerebral Haemorrhage Traumatic                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Clavicle Fracture                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Concussion                                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Drug Toxicity                                   |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Extradural Haematoma                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Eyeball Rupture                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Face Injury                                     |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Facial Bones Fracture                           |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Fall  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Femur Fracture                                  |                |                 |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (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           |
| Head Injury                                     |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 2 / 521 (0.38%) | 0 / 450 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Hip Fracture                                    |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Humerus Fracture                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 2 / 450 (0.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Injury  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Lower Limb Fracture                             |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 2 / 450 (0.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Lumbar Vertebral Fracture                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Open Wound                                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Overdose  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Poisoning                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Road Traffic Accident                           |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Skin Laceration                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Skull Fracture                                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Thermal Burn                                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Traumatic Brain Injury                          |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 2 / 450 (0.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Wrist Fracture                                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Congenital, familial and genetic disorders      |                |                 |                 |
| Odontogenic Cyst                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Cardiac disorders                               |                |                 |                 |
| Acute Myocardial Infarction                     |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| Mitral Valve Prolapse                           |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Pericardial Effusion                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                |                 |                 |
| Balance Disorder                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Brain Stem Infarction                           |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Cerebral Haematoma                              |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Cerebrosclerosis                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Cerebrovascular Accident                        |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Coma  |                |                 |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (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           |
| Complex Partial Seizures                        |                |                 |                 |

|   |                |                  |                 |
|---|----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%)  | 2 / 450 (0.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1            | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0            | 0 / 0           |
| Convulsion                                      |                |                  |                 |
| subjects affected / exposed                     | 2 / 37 (5.41%) | 11 / 521 (2.11%) | 5 / 450 (1.11%) |
| occurrences causally related to treatment / all | 0 / 2          | 1 / 15           | 1 / 6           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0            | 0 / 0           |
| Dizziness                                       |                |                  |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%)  | 0 / 450 (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           |
| Encephalopathy                                  |                |                  |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%)  | 0 / 450 (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           |
| Epilepsy  |                |                  |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 6 / 521 (1.15%)  | 5 / 450 (1.11%) |
| occurrences causally related to treatment / all | 0 / 1          | 2 / 8            | 0 / 5           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0            | 0 / 0           |
| Grand Mal Convulsion                            |                |                  |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%)  | 2 / 450 (0.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1            | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0            | 0 / 0           |
| Haemorrhage Intracranial                        |                |                  |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%)  | 0 / 450 (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           |
| Headache  |                |                  |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%)  | 0 / 450 (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           |
| Loss of Consciousness                           |                |                  |                 |



|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Memory Impairment                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Parkinsonism                                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Partial Seizures                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Postictal State                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 2 / 521 (0.38%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 2           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Psychomotor Hyperactivity                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Speech Disorder                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Status Epilepticus                              |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 7 / 521 (1.34%) | 3 / 450 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 7           | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Temporal Lobe Epilepsy                          |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Transient Ischaemic Attack                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Blood and lymphatic system disorders            |                |                 |                 |
| Anaemia   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Thrombocytopenia                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Ear and labyrinth disorders                     |                |                 |                 |
| Deafness  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Vertigo   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Eye disorders                                   |                |                 |                 |
| Blindness                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                |                 |                 |
| Abdominal Hernia                                |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Enterocolitis                                   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Gastric Ulcer                                   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Gastritis                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Gastrointestinal Haemorrhage                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Inguinal Hernia                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Melaena   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Pancreatitis Acute                              |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 2 / 450 (0.44%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Periproctitis                                   |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Salivary Gland Calculus                         |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Small Intestinal Obstruction                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Vomiting  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Hepatobiliary disorders                         |                |                 |                 |
| Cholecystitis                                   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Cholelithiasis                                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Gallbladder Non-Functioning                     |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Hepatitis                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Jaundice  |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Skin and subcutaneous tissue disorders          |                |                 |                 |
| Rash Generalised                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Scar  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                |                 |                 |
| Calculus Ureteric                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Incontinence                                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Renal Failure Acute                             |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Renal Impairment                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Urinary Retention                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Musculoskeletal and connective tissue           |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| disorders                                       |                |                 |                 |
| Arthritis                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Back Pain                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Bone Pain                                       |                |                 |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (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           |
| Cervical Spinal Stenosis                        |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Groin Pain                                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Intervertebral Disc Disorder                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Lumbar Spinal Stenosis                          |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Musculoskeletal Chest Pain                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Myalgia   |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Neck Pain                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Pain in Extremity                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Spinal Osteoarthritis                           |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Infections and infestations                     |                |                 |                 |
| Appendicitis                                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Bronchopneumonia                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Ear Infection                                   |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Gastroenteritis                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Gastroenteritis Viral                           |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Ovarian Infection                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Pelvic Inflammatory Disease                     |                |                 |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (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           |
| Plasmodium Falciparum Infection                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Pneumonia                                       |                |                 |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 2 / 450 (0.44%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Pneumonia Primary Atypical                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Pyelonephritis                                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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           |
| Pyelonephritis Acute                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Sepsis  |                |                 |                 |



|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 0 / 450 (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>Typhoid Fever</b>                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 521 (0.00%) | 1 / 450 (0.22%) |
| 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>Urinary Tract Infection</b>                  |                |                 |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (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>Metabolism and nutrition disorders</b>       |                |                 |                 |
| <b>Hyponatraemia</b>                            |                |                 |                 |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (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>Serious adverse events</b>  | Carsibamate >800-1000mg |  |  |
| <b>Total subjects affected by serious adverse events</b>                   |                         |  |  |
| subjects affected / exposed  | 0 / 2 (0.00%)           |  |  |
| number of deaths (all causes)  | 0                       |  |  |
| number of deaths resulting from adverse events                             |                         |  |  |
| <b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b> |                         |  |  |
| <b>Adenocarcinoma</b>  |                         |  |  |
| subjects affected / exposed  | 0 / 2 (0.00%)           |  |  |
| occurrences causally related to treatment / all                            | 0 / 0                   |  |  |
| deaths causally related to treatment / all                                 | 0 / 0                   |  |  |
| <b>Basal Cell Carcinoma</b>  |                         |  |  |
| subjects affected / exposed  | 0 / 2 (0.00%)           |  |  |
| occurrences causally related to treatment / all                            | 0 / 0                   |  |  |
| deaths causally related to treatment / all                                 | 0 / 0                   |  |  |
| <b>Breast Cancer</b>   |                         |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Fibroadenoma of Breast                          |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Lip And/Or Oral Cavity Cancer                   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Melanocytic Naevus                              |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Non-Hodgkin's Lymphoma                          |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Oligodendroglioma                               |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Thyroid Cancer                                  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Uterine Leiomyoma                               |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Vascular disorders                              |               |  |  |
| Aneurysm Arteriovenous                          |               |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hypotension                                     |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Surgical and medical procedures                 |               |  |  |
| Arthrodesis                                     |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cardiac Pacemaker Insertion                     |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cataract Operation                              |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Elective Surgery                                |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Endocervical Curettage                          |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hospitalisation                                 |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hysterectomy                                    |               |  |  |

|  |               |  |  |
|--|---------------|--|--|
| subjects affected / exposed                          | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0         |  |  |
| deaths causally related to treatment / all           | 0 / 0         |  |  |
| Medical Device Removal                               |               |  |  |
| subjects affected / exposed                          | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0         |  |  |
| deaths causally related to treatment / all           | 0 / 0         |  |  |
| Nasal Operation                                      |               |  |  |
| subjects affected / exposed                          | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0         |  |  |
| deaths causally related to treatment / all           | 0 / 0         |  |  |
| Neurosurgery   |               |  |  |
| subjects affected / exposed                          | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0         |  |  |
| deaths causally related to treatment / all           | 0 / 0         |  |  |
| Ovarian Cystectomy                                   |               |  |  |
| subjects affected / exposed                          | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0         |  |  |
| deaths causally related to treatment / all           | 0 / 0         |  |  |
| Spinal Fusion Surgery                                |               |  |  |
| subjects affected / exposed                          | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0         |  |  |
| deaths causally related to treatment / all           | 0 / 0         |  |  |
| Surgery  |               |  |  |
| subjects affected / exposed                          | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0         |  |  |
| deaths causally related to treatment / all           | 0 / 0         |  |  |
| Vagal Nerve Stimulator Removal                       |               |  |  |
| subjects affected / exposed                          | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0         |  |  |
| deaths causally related to treatment / all           | 0 / 0         |  |  |
| General disorders and administration site conditions |               |  |  |
| Chest Pain   |               |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Drowning  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pyrexia   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Reproductive system and breast disorders        |               |  |  |
| Benign Prostatic Hyperplasia                    |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Metrorrhagia                                    |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Ovarian Cyst                                    |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Respiratory, thoracic and mediastinal disorders |               |  |  |
| Asphyxia  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pneumonia Aspiration                            |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |

|   |               |  |  |
|---|---------------|--|--|
| Respiratory Distress                            |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Psychiatric disorders                           |               |  |  |
| Abnormal Behaviour                              |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Acute Psychosis                                 |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Aggression                                      |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Agitation                                       |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Anxiety   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Conversion Disorder                             |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Delirium  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Depression                                      |               |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Dysphoria                                       |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hallucination                                   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hypomania                                       |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Major Depression                                |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Psychotic Disorder                              |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Suicide Attempt                                 |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Investigations                                  |               |  |  |
| Diagnostic Procedure                            |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Electroencephalogram                            |               |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Liver Function Test Abnormal                    |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Injury, poisoning and procedural complications  |               |  |  |
| Accidental Exposure                             |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Ankle Fracture                                  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Brain Contusion                                 |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cerebral Haemorrhage Traumatic                  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Clavicle Fracture                               |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Concussion                                      |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Drug Toxicity                                   |               |  |  |



|   |               |  |  |  |
|---|---------------|--|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Extradural Haematoma                            |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Eyeball Rupture                                 |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Face Injury                                     |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Facial Bones Fracture                           |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Fall  |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Femur Fracture                                  |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Head Injury                                     |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Hip Fracture                                    |               |  |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Humerus Fracture                                |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Injury  |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Lower Limb Fracture                             |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Lumbar Vertebral Fracture                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Open Wound                                      |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Overdose  |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Poisoning                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Road Traffic Accident                           |               |  |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Skin Laceration                                 |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Skull Fracture                                  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Thermal Burn                                    |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Traumatic Brain Injury                          |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Wrist Fracture                                  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Congenital, familial and genetic disorders      |               |  |  |
| Odontogenic Cyst                                |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cardiac disorders                               |               |  |  |
| Acute Myocardial Infarction                     |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |

|   |               |  |  |
|---|---------------|--|--|
| Mitral Valve Prolapse                           |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pericardial Effusion                            |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Nervous system disorders                        |               |  |  |
| Balance Disorder                                |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Brain Stem Infarction                           |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cerebral Haematoma                              |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cerebroscclerosis                               |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cerebrovascular Accident                        |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Coma  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Complex Partial Seizures                        |               |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Convulsion                                      |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Dizziness                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Encephalopathy                                  |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Epilepsy  |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Grand Mal Convulsion                            |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Haemorrhage Intracranial                        |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Headache  |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Loss of Consciousness                           |               |  |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Memory Impairment                               |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Parkinsonism                                    |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Partial Seizures                                |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Postictal State                                 |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Psychomotor Hyperactivity                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Speech Disorder                                 |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Status Epilepticus                              |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Temporal Lobe Epilepsy                          |               |  |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Transient Ischaemic Attack                      |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Blood and lymphatic system disorders            |               |  |  |
| Anaemia   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Thrombocytopenia                                |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Ear and labyrinth disorders                     |               |  |  |
| Deafness  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Vertigo   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Eye disorders                                   |               |  |  |
| Blindness                                       |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Gastrointestinal disorders                      |               |  |  |
| Abdominal Hernia                                |               |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Enterocolitis                                   |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Gastric Ulcer                                   |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Gastritis                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Gastrointestinal Haemorrhage                    |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Inguinal Hernia                                 |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Melaena   |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Pancreatitis Acute                              |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Periproctitis                                   |               |  |  |  |



|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Salivary Gland Calculus                         |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Small Intestinal Obstruction                    |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Vomiting  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hepatobiliary disorders                         |               |  |  |
| Cholecystitis                                   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cholelithiasis                                  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Gallbladder Non-Functioning                     |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hepatitis                                       |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Jaundice  |               |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Skin and subcutaneous tissue disorders          |               |  |  |
| Rash Generalised                                |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Scar  |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Renal and urinary disorders                     |               |  |  |
| Calculus Ureteric                               |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Incontinence                                    |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Renal Failure Acute                             |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Renal Impairment                                |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Urinary Retention                               |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Musculoskeletal and connective tissue           |               |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| disorders                                       |               |  |  |  |
| Arthritis                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Back Pain                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Bone Pain                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Cervical Spinal Stenosis                        |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Groin Pain                                      |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Intervertebral Disc Disorder                    |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Lumbar Spinal Stenosis                          |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Musculoskeletal Chest Pain                      |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Myalgia   |               |  |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Neck Pain                                       |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pain in Extremity                               |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Spinal Osteoarthritis                           |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Infections and infestations                     |               |  |  |
| Appendicitis                                    |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Bronchopneumonia                                |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Ear Infection                                   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Gastroenteritis                                 |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Gastroenteritis Viral                           |               |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Ovarian Infection                               |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Pelvic Inflammatory Disease                     |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Plasmodium Falciparum Infection                 |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Pneumonia                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Pneumonia Primary Atypical                      |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Pyelonephritis                                  |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Pyelonephritis Acute                            |               |  |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Sepsis  |               |  |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Typhoid Fever                                   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Urinary Tract Infection                         |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Metabolism and nutrition disorders              |               |  |  |
| Hyponatraemia                                   |               |  |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |

Frequency threshold for reporting non-serious adverse events: 1 %

| <b>Non-serious adverse events</b>                     | Carsibamate <400 mg | Carsibamate 400- <600mg | Carisbamate 600-800 mg |
|---|---------------------|-------------------------|------------------------|
| Total subjects affected by non-serious adverse events |                     |                         |                        |
| subjects affected / exposed                           | 32 / 37 (86.49%)    | 290 / 521 (55.66%)      | 314 / 450 (69.78%)     |
| Vascular disorders                                    |                     |                         |                        |
| Hot Flush   |                     |                         |                        |
| subjects affected / exposed                           | 1 / 37 (2.70%)      | 1 / 521 (0.19%)         | 0 / 450 (0.00%)        |
| occurrences (all)                                     | 1                   | 3                       | 0                      |
| Hypertension  |                     |                         |                        |
| subjects affected / exposed                           | 1 / 37 (2.70%)      | 8 / 521 (1.54%)         | 15 / 450 (3.33%)       |
| occurrences (all)                                     | 15                  | 26                      | 34                     |
| Hypotension   |                     |                         |                        |
| subjects affected / exposed                           | 1 / 37 (2.70%)      | 3 / 521 (0.58%)         | 1 / 450 (0.22%)        |
| occurrences (all)                                     | 3                   | 10                      | 1                      |
| General disorders and administration site conditions  |                     |                         |                        |

|                             |                 |                  |                  |
|-----------------------------|-----------------|------------------|------------------|
| Asthenia                    |                 |                  |                  |
| subjects affected / exposed | 2 / 37 (5.41%)  | 16 / 521 (3.07%) | 19 / 450 (4.22%) |
| occurrences (all)           | 4               | 25               | 21               |
| Chest Discomfort            |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 5 / 521 (0.96%)  | 5 / 450 (1.11%)  |
| occurrences (all)           | 1               | 8                | 5                |
| Chest Pain                  |                 |                  |                  |
| subjects affected / exposed | 2 / 37 (5.41%)  | 5 / 521 (0.96%)  | 7 / 450 (1.56%)  |
| occurrences (all)           | 32              | 5                | 11               |
| Chills                      |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 1 / 450 (0.22%)  |
| occurrences (all)           | 1               | 1                | 1                |
| Fatigue                     |                 |                  |                  |
| subjects affected / exposed | 8 / 37 (21.62%) | 25 / 521 (4.80%) | 31 / 450 (6.89%) |
| occurrences (all)           | 10              | 30               | 45               |
| Feeling Cold                |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)           | 1               | 0                | 0                |
| Gait Disturbance            |                 |                  |                  |
| subjects affected / exposed | 0 / 37 (0.00%)  | 3 / 521 (0.58%)  | 5 / 450 (1.11%)  |
| occurrences (all)           | 0               | 3                | 7                |
| Irritability                |                 |                  |                  |
| subjects affected / exposed | 3 / 37 (8.11%)  | 16 / 521 (3.07%) | 10 / 450 (2.22%) |
| occurrences (all)           | 4               | 31               | 11               |
| Oedema Peripheral           |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 3 / 521 (0.58%)  | 4 / 450 (0.89%)  |
| occurrences (all)           | 1               | 3                | 5                |
| Pyrexia                     |                 |                  |                  |
| subjects affected / exposed | 4 / 37 (10.81%) | 17 / 521 (3.26%) | 26 / 450 (5.78%) |
| occurrences (all)           | 4               | 24               | 29               |
| Sense of Oppression         |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)           | 1               | 0                | 0                |
| Immune system disorders     |                 |                  |                  |
| Seasonal Allergy            |                 |                  |                  |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 37 (2.70%)<br>1 | 1 / 521 (0.19%)<br>1 | 4 / 450 (0.89%)<br>6 |
| Reproductive system and breast disorders         |                     |                      |                      |
| Dysmenorrhoea                                    |                     |                      |                      |
| subjects affected / exposed                      | 1 / 37 (2.70%)      | 3 / 521 (0.58%)      | 2 / 450 (0.44%)      |
| occurrences (all)                                | 1                   | 29                   | 7                    |
| Hypomenorrhoea                                   |                     |                      |                      |
| subjects affected / exposed                      | 1 / 37 (2.70%)      | 0 / 521 (0.00%)      | 0 / 450 (0.00%)      |
| occurrences (all)                                | 1                   | 0                    | 0                    |
| Respiratory, thoracic and mediastinal disorders  |                     |                      |                      |
| Bronchitis Chronic                               |                     |                      |                      |
| subjects affected / exposed                      | 1 / 37 (2.70%)      | 0 / 521 (0.00%)      | 0 / 450 (0.00%)      |
| occurrences (all)                                | 1                   | 0                    | 0                    |
| Cough  |                     |                      |                      |
| subjects affected / exposed                      | 0 / 37 (0.00%)      | 7 / 521 (1.34%)      | 10 / 450 (2.22%)     |
| occurrences (all)                                | 0                   | 7                    | 10                   |
| Dyspnoea   |                     |                      |                      |
| subjects affected / exposed                      | 1 / 37 (2.70%)      | 2 / 521 (0.38%)      | 4 / 450 (0.89%)      |
| occurrences (all)                                | 1                   | 2                    | 4                    |
| Epistaxis  |                     |                      |                      |
| subjects affected / exposed                      | 1 / 37 (2.70%)      | 2 / 521 (0.38%)      | 4 / 450 (0.89%)      |
| occurrences (all)                                | 1                   | 2                    | 7                    |
| Hyperventilation                                 |                     |                      |                      |
| subjects affected / exposed                      | 1 / 37 (2.70%)      | 0 / 521 (0.00%)      | 1 / 450 (0.22%)      |
| occurrences (all)                                | 1                   | 0                    | 2                    |
| Nasal Congestion                                 |                     |                      |                      |
| subjects affected / exposed                      | 1 / 37 (2.70%)      | 1 / 521 (0.19%)      | 2 / 450 (0.44%)      |
| occurrences (all)                                | 1                   | 1                    | 2                    |
| Rhinitis Allergic                                |                     |                      |                      |
| subjects affected / exposed                      | 1 / 37 (2.70%)      | 0 / 521 (0.00%)      | 0 / 450 (0.00%)      |
| occurrences (all)                                | 1                   | 0                    | 0                    |
| Oropharyngeal Pain                               |                     |                      |                      |
| subjects affected / exposed                      | 2 / 37 (5.41%)      | 6 / 521 (1.15%)      | 8 / 450 (1.78%)      |
| occurrences (all)                                | 3                   | 6                    | 9                    |
| Rhinorrhoea                                      |                     |                      |                      |



|                                 |                 |                  |                  |
|---------------------------------|-----------------|------------------|------------------|
| subjects affected / exposed     | 1 / 37 (2.70%)  | 3 / 521 (0.58%)  | 2 / 450 (0.44%)  |
| occurrences (all)               | 1               | 3                | 2                |
| Sinus Congestion                |                 |                  |                  |
| subjects affected / exposed     | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 2 / 450 (0.44%)  |
| occurrences (all)               | 1               | 0                | 2                |
| Psychiatric disorders           |                 |                  |                  |
| Aggression                      |                 |                  |                  |
| subjects affected / exposed     | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 3 / 450 (0.67%)  |
| occurrences (all)               | 1               | 1                | 3                |
| Anxiety                         |                 |                  |                  |
| subjects affected / exposed     | 3 / 37 (8.11%)  | 9 / 521 (1.73%)  | 15 / 450 (3.33%) |
| occurrences (all)               | 4               | 9                | 20               |
| Depression                      |                 |                  |                  |
| subjects affected / exposed     | 1 / 37 (2.70%)  | 10 / 521 (1.92%) | 16 / 450 (3.56%) |
| occurrences (all)               | 1               | 11               | 19               |
| Disturbance in Social Behaviour |                 |                  |                  |
| subjects affected / exposed     | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)               | 1               | 0                | 0                |
| Dysphoria                       |                 |                  |                  |
| subjects affected / exposed     | 0 / 37 (0.00%)  | 7 / 521 (1.34%)  | 0 / 450 (0.00%)  |
| occurrences (all)               | 0               | 7                | 0                |
| Insomnia                        |                 |                  |                  |
| subjects affected / exposed     | 4 / 37 (10.81%) | 26 / 521 (4.99%) | 26 / 450 (5.78%) |
| occurrences (all)               | 6               | 42               | 29               |
| Libido Decreased                |                 |                  |                  |
| subjects affected / exposed     | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 0 / 450 (0.00%)  |
| occurrences (all)               | 1               | 1                | 0                |
| Nervousness                     |                 |                  |                  |
| subjects affected / exposed     | 0 / 37 (0.00%)  | 7 / 521 (1.34%)  | 1 / 450 (0.22%)  |
| occurrences (all)               | 0               | 8                | 1                |
| Stress                          |                 |                  |                  |
| subjects affected / exposed     | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)               | 1               | 0                | 0                |
| Suicidal Ideation               |                 |                  |                  |
| subjects affected / exposed     | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 5 / 450 (1.11%)  |
| occurrences (all)               | 1               | 1                | 5                |

|  |                |                  |                  |
|--|----------------|------------------|------------------|
| Investigations                                 |                |                  |                  |
| Alanine Aminotransferase Increased             |                |                  |                  |
| subjects affected / exposed                    | 0 / 37 (0.00%) | 8 / 521 (1.54%)  | 7 / 450 (1.56%)  |
| occurrences (all)                              | 0              | 9                | 7                |
| Aspartate Aminotransferase Increased           |                |                  |                  |
| subjects affected / exposed                    | 0 / 37 (0.00%) | 4 / 521 (0.77%)  | 6 / 450 (1.33%)  |
| occurrences (all)                              | 0              | 5                | 6                |
| Blood Pressure Increased                       |                |                  |                  |
| subjects affected / exposed                    | 1 / 37 (2.70%) | 1 / 521 (0.19%)  | 4 / 450 (0.89%)  |
| occurrences (all)                              | 1              | 1                | 9                |
| Weight Decreased                               |                |                  |                  |
| subjects affected / exposed                    | 0 / 37 (0.00%) | 7 / 521 (1.34%)  | 12 / 450 (2.67%) |
| occurrences (all)                              | 0              | 11               | 12               |
| Weight Increased                               |                |                  |                  |
| subjects affected / exposed                    | 0 / 37 (0.00%) | 2 / 521 (0.38%)  | 5 / 450 (1.11%)  |
| occurrences (all)                              | 0              | 2                | 5                |
| Injury, poisoning and procedural complications |                |                  |                  |
| Contusion                                      |                |                  |                  |
| subjects affected / exposed                    | 2 / 37 (5.41%) | 10 / 521 (1.92%) | 13 / 450 (2.89%) |
| occurrences (all)                              | 3              | 11               | 19               |
| Excoriation                                    |                |                  |                  |
| subjects affected / exposed                    | 1 / 37 (2.70%) | 5 / 521 (0.96%)  | 8 / 450 (1.78%)  |
| occurrences (all)                              | 1              | 5                | 9                |
| Fall   |                |                  |                  |
| subjects affected / exposed                    | 0 / 37 (0.00%) | 1 / 521 (0.19%)  | 7 / 450 (1.56%)  |
| occurrences (all)                              | 0              | 1                | 10               |
| Head Injury                                    |                |                  |                  |
| subjects affected / exposed                    | 0 / 37 (0.00%) | 6 / 521 (1.15%)  | 1 / 450 (0.22%)  |
| occurrences (all)                              | 0              | 7                | 6                |
| Joint Injury                                   |                |                  |                  |
| subjects affected / exposed                    | 1 / 37 (2.70%) | 1 / 521 (0.19%)  | 4 / 450 (0.89%)  |
| occurrences (all)                              | 1              | 1                | 4                |
| Laceration                                     |                |                  |                  |
| subjects affected / exposed                    | 0 / 37 (0.00%) | 2 / 521 (0.38%)  | 12 / 450 (2.67%) |
| occurrences (all)                              | 0              | 2                | 16               |
| Ligament Sprain                                |                |                  |                  |

|   |                     |                      |                        |
|---|---------------------|----------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)  | 1 / 37 (2.70%)<br>1 | 0 / 521 (0.00%)<br>0 | 0 / 450 (0.00%)<br>0   |
| Skin Laceration<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 37 (2.70%)<br>1 | 4 / 521 (0.77%)<br>8 | 16 / 450 (3.56%)<br>19 |
| Thermal Burn<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 37 (0.00%)<br>0 | 5 / 521 (0.96%)<br>5 | 6 / 450 (1.33%)<br>6   |
| Wound<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 37 (2.70%)<br>1 | 1 / 521 (0.19%)<br>1 | 2 / 450 (0.44%)<br>2   |
| Cardiac disorders<br>Cardiac Discomfort<br>subjects affected / exposed<br>occurrences (all) | 1 / 37 (2.70%)<br>1 | 0 / 521 (0.00%)<br>0 | 0 / 450 (0.00%)<br>0   |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 37 (0.00%)<br>0 | 6 / 521 (1.15%)<br>6 | 3 / 450 (0.67%)<br>4   |
| Nervous system disorders<br>Ageusia<br>subjects affected / exposed<br>occurrences (all)     | 1 / 37 (2.70%)<br>1 | 0 / 521 (0.00%)<br>0 | 0 / 450 (0.00%)<br>0   |
| Agnosia<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 37 (2.70%)<br>1 | 0 / 521 (0.00%)<br>0 | 0 / 450 (0.00%)<br>0   |
| Amnesia<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 37 (2.70%)<br>1 | 5 / 521 (0.96%)<br>5 | 3 / 450 (0.67%)<br>8   |
| Ataxia<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 37 (0.00%)<br>0 | 2 / 521 (0.38%)<br>2 | 9 / 450 (2.00%)<br>12  |
| Balance Disorder<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 37 (0.00%)<br>0 | 6 / 521 (1.15%)<br>7 | 9 / 450 (2.00%)<br>12  |
| Convulsion  |                     |                      |                        |

|                             |                  |                   |                   |
|-----------------------------|------------------|-------------------|-------------------|
| subjects affected / exposed | 5 / 37 (13.51%)  | 19 / 521 (3.65%)  | 33 / 450 (7.33%)  |
| occurrences (all)           | 5                | 24                | 44                |
| Dizziness                   |                  |                   |                   |
| subjects affected / exposed | 11 / 37 (29.73%) | 57 / 521 (10.94%) | 87 / 450 (19.33%) |
| occurrences (all)           | 26               | 118               | 312               |
| Disturbance in Attention    |                  |                   |                   |
| subjects affected / exposed | 0 / 37 (0.00%)   | 10 / 521 (1.92%)  | 7 / 450 (1.56%)   |
| occurrences (all)           | 0                | 11                | 8                 |
| Facial Palsy                |                  |                   |                   |
| subjects affected / exposed | 1 / 37 (2.70%)   | 0 / 521 (0.00%)   | 0 / 450 (0.00%)   |
| occurrences (all)           | 1                | 0                 | 0                 |
| Head Discomfort             |                  |                   |                   |
| subjects affected / exposed | 1 / 37 (2.70%)   | 0 / 521 (0.00%)   | 2 / 450 (0.44%)   |
| occurrences (all)           | 1                | 0                 | 2                 |
| Headache                    |                  |                   |                   |
| subjects affected / exposed | 10 / 37 (27.03%) | 91 / 521 (17.47%) | 83 / 450 (18.44%) |
| occurrences (all)           | 48               | 646               | 514               |
| Hypoaesthesia               |                  |                   |                   |
| subjects affected / exposed | 0 / 37 (0.00%)   | 5 / 521 (0.96%)   | 5 / 450 (1.11%)   |
| occurrences (all)           | 0                | 7                 | 6                 |
| Hypotonia                   |                  |                   |                   |
| subjects affected / exposed | 1 / 37 (2.70%)   | 0 / 521 (0.00%)   | 0 / 450 (0.00%)   |
| occurrences (all)           | 1                | 0                 | 0                 |
| Lethargy                    |                  |                   |                   |
| subjects affected / exposed | 1 / 37 (2.70%)   | 3 / 521 (0.58%)   | 3 / 450 (0.67%)   |
| occurrences (all)           | 1                | 4                 | 3                 |
| Memory Impairment           |                  |                   |                   |
| subjects affected / exposed | 0 / 37 (0.00%)   | 8 / 521 (1.54%)   | 11 / 450 (2.44%)  |
| occurrences (all)           | 0                | 8                 | 13                |
| Migraine                    |                  |                   |                   |
| subjects affected / exposed | 1 / 37 (2.70%)   | 4 / 521 (0.77%)   | 9 / 450 (2.00%)   |
| occurrences (all)           | 1                | 5                 | 19                |
| Nystagmus                   |                  |                   |                   |
| subjects affected / exposed | 0 / 37 (0.00%)   | 4 / 521 (0.77%)   | 5 / 450 (1.11%)   |
| occurrences (all)           | 0                | 4                 | 9                 |
| Paraesthesia                |                  |                   |                   |

|                                      |                |                  |                  |
|--------------------------------------|----------------|------------------|------------------|
| subjects affected / exposed          | 1 / 37 (2.70%) | 7 / 521 (1.34%)  | 7 / 450 (1.56%)  |
| occurrences (all)                    | 1              | 10               | 8                |
| Poor Quality Sleep                   |                |                  |                  |
| subjects affected / exposed          | 1 / 37 (2.70%) | 0 / 521 (0.00%)  | 1 / 450 (0.22%)  |
| occurrences (all)                    | 1              | 0                | 1                |
| Postictal State                      |                |                  |                  |
| subjects affected / exposed          | 1 / 37 (2.70%) | 0 / 521 (0.00%)  | 1 / 450 (0.22%)  |
| occurrences (all)                    | 1              | 0                | 1                |
| Sedation                             |                |                  |                  |
| subjects affected / exposed          | 1 / 37 (2.70%) | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)                    | 1              | 0                | 0                |
| Simple Partial Seizures              |                |                  |                  |
| subjects affected / exposed          | 1 / 37 (2.70%) | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)                    | 2              | 0                | 0                |
| Somnolence                           |                |                  |                  |
| subjects affected / exposed          | 0 / 37 (0.00%) | 24 / 521 (4.61%) | 37 / 450 (8.22%) |
| occurrences (all)                    | 0              | 26               | 47               |
| Tension Headache                     |                |                  |                  |
| subjects affected / exposed          | 1 / 37 (2.70%) | 1 / 521 (0.19%)  | 2 / 450 (0.44%)  |
| occurrences (all)                    | 1              | 1                | 3                |
| Tremor                               |                |                  |                  |
| subjects affected / exposed          | 0 / 37 (0.00%) | 8 / 521 (1.54%)  | 12 / 450 (2.67%) |
| occurrences (all)                    | 0              | 8                | 26               |
| Blood and lymphatic system disorders |                |                  |                  |
| Anaemia                              |                |                  |                  |
| subjects affected / exposed          | 1 / 37 (2.70%) | 7 / 521 (1.34%)  | 3 / 450 (0.67%)  |
| occurrences (all)                    | 1              | 10               | 3                |
| Ear and labyrinth disorders          |                |                  |                  |
| Ear Pain                             |                |                  |                  |
| subjects affected / exposed          | 1 / 37 (2.70%) | 2 / 521 (0.38%)  | 3 / 450 (0.67%)  |
| occurrences (all)                    | 2              | 2                | 4                |
| Vertigo                              |                |                  |                  |
| subjects affected / exposed          | 0 / 37 (0.00%) | 10 / 521 (1.92%) | 11 / 450 (2.44%) |
| occurrences (all)                    | 0              | 17               | 30               |
| Eye disorders                        |                |                  |                  |

|                             |                 |                  |                  |
|-----------------------------|-----------------|------------------|------------------|
| Cataract                    |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 3 / 450 (0.67%)  |
| occurrences (all)           | 2               | 1                | 3                |
| Diplopia                    |                 |                  |                  |
| subjects affected / exposed | 0 / 37 (0.00%)  | 5 / 521 (0.96%)  | 16 / 450 (3.56%) |
| occurrences (all)           | 0               | 6                | 46               |
| Eye Movement Disorder       |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)           | 1               | 0                | 0                |
| Lacrimation Increased       |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 2 / 521 (0.38%)  | 0 / 450 (0.00%)  |
| occurrences (all)           | 1               | 2                | 0                |
| Vision Blurred              |                 |                  |                  |
| subjects affected / exposed | 3 / 37 (8.11%)  | 9 / 521 (1.73%)  | 20 / 450 (4.44%) |
| occurrences (all)           | 9               | 11               | 33               |
| Visual Acuity Reduced       |                 |                  |                  |
| subjects affected / exposed | 0 / 37 (0.00%)  | 1 / 521 (0.19%)  | 5 / 450 (1.11%)  |
| occurrences (all)           | 0               | 1                | 5                |
| Visual Impairment           |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 1 / 450 (0.22%)  |
| occurrences (all)           | 1               | 1                | 1                |
| Gastrointestinal disorders  |                 |                  |                  |
| Abdominal Pain              |                 |                  |                  |
| subjects affected / exposed | 2 / 37 (5.41%)  | 6 / 521 (1.15%)  | 9 / 450 (2.00%)  |
| occurrences (all)           | 5               | 59               | 10               |
| Abdominal Pain Lower        |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 1 / 450 (0.22%)  |
| occurrences (all)           | 1               | 1                | 1                |
| Abdominal Pain Upper        |                 |                  |                  |
| subjects affected / exposed | 4 / 37 (10.81%) | 11 / 521 (2.11%) | 13 / 450 (2.89%) |
| occurrences (all)           | 4               | 22               | 17               |
| Aphthous Stomatitis         |                 |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 2 / 450 (0.44%)  |
| occurrences (all)           | 1               | 1                | 7                |
| Constipation                |                 |                  |                  |

|  |                 |                  |                  |
|--|-----------------|------------------|------------------|
| subjects affected / exposed            | 3 / 37 (8.11%)  | 14 / 521 (2.69%) | 12 / 450 (2.67%) |
| occurrences (all)                      | 3               | 15               | 15               |
| Diarrhoea                              |                 |                  |                  |
| subjects affected / exposed            | 3 / 37 (8.11%)  | 20 / 521 (3.84%) | 23 / 450 (5.11%) |
| occurrences (all)                      | 6               | 26               | 32               |
| Duodenitis                             |                 |                  |                  |
| subjects affected / exposed            | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)                      | 1               | 0                | 0                |
| Dyspepsia                              |                 |                  |                  |
| subjects affected / exposed            | 1 / 37 (2.70%)  | 9 / 521 (1.73%)  | 20 / 450 (4.44%) |
| occurrences (all)                      | 1               | 14               | 35               |
| Gastric Ulcer                          |                 |                  |                  |
| subjects affected / exposed            | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 0 / 450 (0.00%)  |
| occurrences (all)                      | 1               | 1                | 0                |
| Gastritis                              |                 |                  |                  |
| subjects affected / exposed            | 1 / 37 (2.70%)  | 9 / 521 (1.73%)  | 4 / 450 (0.89%)  |
| occurrences (all)                      | 1               | 10               | 4                |
| Gastrooesophageal Reflux Disease       |                 |                  |                  |
| subjects affected / exposed            | 0 / 37 (0.00%)  | 1 / 521 (0.19%)  | 6 / 450 (1.33%)  |
| occurrences (all)                      | 0               | 1                | 7                |
| Nausea                                 |                 |                  |                  |
| subjects affected / exposed            | 5 / 37 (13.51%) | 26 / 521 (4.99%) | 27 / 450 (6.00%) |
| occurrences (all)                      | 6               | 34               | 40               |
| Periodontitis                          |                 |                  |                  |
| subjects affected / exposed            | 1 / 37 (2.70%)  | 2 / 521 (0.38%)  | 2 / 450 (0.44%)  |
| occurrences (all)                      | 1               | 2                | 2                |
| Rectal Haemorrhage                     |                 |                  |                  |
| subjects affected / exposed            | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)                      | 1               | 0                | 0                |
| Toothache                              |                 |                  |                  |
| subjects affected / exposed            | 1 / 37 (2.70%)  | 5 / 521 (0.96%)  | 5 / 450 (1.11%)  |
| occurrences (all)                      | 1               | 8                | 5                |
| Vomiting                               |                 |                  |                  |
| subjects affected / exposed            | 4 / 37 (10.81%) | 26 / 521 (4.99%) | 21 / 450 (4.67%) |
| occurrences (all)                      | 10              | 29               | 34               |
| Skin and subcutaneous tissue disorders |                 |                  |                  |

|   |                |                 |                  |
|---|----------------|-----------------|------------------|
| Alopecia  |                |                 |                  |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 8 / 521 (1.54%) | 6 / 450 (1.33%)  |
| occurrences (all)                               | 0              | 8               | 7                |
| Decubitus Ulcer                                 |                |                 |                  |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0                |
| Dermal Cyst                                     |                |                 |                  |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0                |
| Eczema  |                |                 |                  |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 7 / 521 (1.34%) | 5 / 450 (1.11%)  |
| occurrences (all)                               | 0              | 7               | 5                |
| Hypoaesthesia Facial                            |                |                 |                  |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0                |
| Rash  |                |                 |                  |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 9 / 521 (1.73%) | 14 / 450 (3.11%) |
| occurrences (all)                               | 0              | 11              | 17               |
| Pruritus  |                |                 |                  |
| subjects affected / exposed                     | 2 / 37 (5.41%) | 3 / 521 (0.58%) | 8 / 450 (1.78%)  |
| occurrences (all)                               | 3              | 3               | 8                |
| Urticaria                                       |                |                 |                  |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 3 / 521 (0.58%) | 5 / 450 (1.11%)  |
| occurrences (all)                               | 0              | 3               | 5                |
| Renal and urinary disorders                     |                |                 |                  |
| Dysuria   |                |                 |                  |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 1 / 521 (0.19%) | 5 / 450 (1.11%)  |
| occurrences (all)                               | 0              | 1               | 5                |
| Polyuria  |                |                 |                  |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 1 / 521 (0.19%) | 0 / 450 (0.00%)  |
| occurrences (all)                               | 1              | 1               | 0                |
| Urinary Tract Pain                              |                |                 |                  |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 521 (0.00%) | 0 / 450 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0                |
| Musculoskeletal and connective tissue disorders |                |                 |                  |



|                             |                |                  |                  |
|-----------------------------|----------------|------------------|------------------|
| Arthralgia                  |                |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%) | 6 / 521 (1.15%)  | 15 / 450 (3.33%) |
| occurrences (all)           | 3              | 10               | 17               |
| Back Pain                   |                |                  |                  |
| subjects affected / exposed | 2 / 37 (5.41%) | 17 / 521 (3.26%) | 22 / 450 (4.89%) |
| occurrences (all)           | 2              | 21               | 38               |
| Bone Pain                   |                |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%) | 2 / 521 (0.38%)  | 2 / 450 (0.44%)  |
| occurrences (all)           | 1              | 35               | 2                |
| Flank Pain                  |                |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 521 (0.00%)  | 1 / 450 (0.22%)  |
| occurrences (all)           | 1              | 0                | 1                |
| Muscle Spasms               |                |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%) | 2 / 521 (0.38%)  | 0 / 450 (0.00%)  |
| occurrences (all)           | 1              | 2                | 0                |
| Musculoskeletal Pain        |                |                  |                  |
| subjects affected / exposed | 3 / 37 (8.11%) | 4 / 521 (0.77%)  | 8 / 450 (1.78%)  |
| occurrences (all)           | 3              | 7                | 8                |
| Musculoskeletal Stiffness   |                |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0                |
| Myalgia                     |                |                  |                  |
| subjects affected / exposed | 0 / 37 (0.00%) | 10 / 521 (1.92%) | 11 / 450 (2.44%) |
| occurrences (all)           | 0              | 15               | 14               |
| Neck Pain                   |                |                  |                  |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 521 (0.38%)  | 1 / 450 (0.22%)  |
| occurrences (all)           | 2              | 2                | 1                |
| Pain in Extremity           |                |                  |                  |
| subjects affected / exposed | 2 / 37 (5.41%) | 6 / 521 (1.15%)  | 13 / 450 (2.89%) |
| occurrences (all)           | 2              | 6                | 13               |
| Tenosynovitis               |                |                  |                  |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0                |
| Infections and infestations |                |                  |                  |
| Bronchitis                  |                |                  |                  |

|                                   |                 |                  |                   |
|-----------------------------------|-----------------|------------------|-------------------|
| subjects affected / exposed       | 2 / 37 (5.41%)  | 2 / 521 (0.38%)  | 9 / 450 (2.00%)   |
| occurrences (all)                 | 3               | 4                | 12                |
| Candidiasis                       |                 |                  |                   |
| subjects affected / exposed       | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 0 / 450 (0.00%)   |
| occurrences (all)                 | 2               | 0                | 0                 |
| Ear Infection                     |                 |                  |                   |
| subjects affected / exposed       | 0 / 37 (0.00%)  | 1 / 521 (0.19%)  | 7 / 450 (1.56%)   |
| occurrences (all)                 | 0               | 1                | 8                 |
| Gastroenteritis                   |                 |                  |                   |
| subjects affected / exposed       | 0 / 37 (0.00%)  | 2 / 521 (0.38%)  | 6 / 450 (1.33%)   |
| occurrences (all)                 | 0               | 2                | 8                 |
| Gastroenteritis Viral             |                 |                  |                   |
| subjects affected / exposed       | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 4 / 450 (0.89%)   |
| occurrences (all)                 | 2               | 2                | 4                 |
| Influenza                         |                 |                  |                   |
| subjects affected / exposed       | 4 / 37 (10.81%) | 9 / 521 (1.73%)  | 19 / 450 (4.22%)  |
| occurrences (all)                 | 4               | 10               | 26                |
| Laryngitis                        |                 |                  |                   |
| subjects affected / exposed       | 1 / 37 (2.70%)  | 1 / 521 (0.19%)  | 1 / 450 (0.22%)   |
| occurrences (all)                 | 1               | 1                | 1                 |
| Nasopharyngitis                   |                 |                  |                   |
| subjects affected / exposed       | 7 / 37 (18.92%) | 37 / 521 (7.10%) | 46 / 450 (10.22%) |
| occurrences (all)                 | 10              | 60               | 84                |
| Pharyngitis                       |                 |                  |                   |
| subjects affected / exposed       | 0 / 37 (0.00%)  | 9 / 521 (1.73%)  | 12 / 450 (2.67%)  |
| occurrences (all)                 | 0               | 9                | 14                |
| Sinusitis                         |                 |                  |                   |
| subjects affected / exposed       | 1 / 37 (2.70%)  | 3 / 521 (0.58%)  | 7 / 450 (1.56%)   |
| occurrences (all)                 | 3               | 3                | 9                 |
| Tonsillitis                       |                 |                  |                   |
| subjects affected / exposed       | 1 / 37 (2.70%)  | 0 / 521 (0.00%)  | 1 / 450 (0.22%)   |
| occurrences (all)                 | 1               | 0                | 1                 |
| Upper Respiratory Tract Infection |                 |                  |                   |
| subjects affected / exposed       | 1 / 37 (2.70%)  | 21 / 521 (4.03%) | 60 / 450 (13.33%) |
| occurrences (all)                 | 1               | 30               | 102               |
| Urinary Tract Infection           |                 |                  |                   |

|                                    |                |                  |                  |
|------------------------------------|----------------|------------------|------------------|
| subjects affected / exposed        | 1 / 37 (2.70%) | 10 / 521 (1.92%) | 19 / 450 (4.22%) |
| occurrences (all)                  | 2              | 13               | 21               |
| Viral Infection                    |                |                  |                  |
| subjects affected / exposed        | 0 / 37 (0.00%) | 0 / 521 (0.00%)  | 8 / 450 (1.78%)  |
| occurrences (all)                  | 0              | 0                | 10               |
| Metabolism and nutrition disorders |                |                  |                  |
| Appetite Disorder                  |                |                  |                  |
| subjects affected / exposed        | 1 / 37 (2.70%) | 1 / 521 (0.19%)  | 1 / 450 (0.22%)  |
| occurrences (all)                  | 1              | 1                | 1                |
| Decreased Appetite                 |                |                  |                  |
| subjects affected / exposed        | 3 / 37 (8.11%) | 20 / 521 (3.84%) | 14 / 450 (3.11%) |
| occurrences (all)                  | 4              | 25               | 15               |
| Hypercholesterolaemia              |                |                  |                  |
| subjects affected / exposed        | 0 / 37 (0.00%) | 1 / 521 (0.19%)  | 5 / 450 (1.11%)  |
| occurrences (all)                  | 0              | 1                | 6                |
| Hyponatraemia                      |                |                  |                  |
| subjects affected / exposed        | 1 / 37 (2.70%) | 1 / 521 (0.19%)  | 2 / 450 (0.44%)  |
| occurrences (all)                  | 1              | 1                | 2                |
| Polydipsia                         |                |                  |                  |
| subjects affected / exposed        | 1 / 37 (2.70%) | 0 / 521 (0.00%)  | 0 / 450 (0.00%)  |
| occurrences (all)                  | 1              | 0                | 0                |

|   |                         |  |  |
|---|-------------------------|--|--|
| <b>Non-serious adverse events</b>                     | Carsibamate >800-1000mg |  |  |
| Total subjects affected by non-serious adverse events |                         |  |  |
| subjects affected / exposed                           | 2 / 2 (100.00%)         |  |  |
| Vascular disorders                                    |                         |  |  |
| Hot Flush   |                         |  |  |
| subjects affected / exposed                           | 0 / 2 (0.00%)           |  |  |
| occurrences (all)                                     | 0                       |  |  |
| Hypertension  |                         |  |  |
| subjects affected / exposed                           | 0 / 2 (0.00%)           |  |  |
| occurrences (all)                                     | 0                       |  |  |
| Hypotension   |                         |  |  |
| subjects affected / exposed                           | 0 / 2 (0.00%)           |  |  |
| occurrences (all)                                     | 0                       |  |  |
| General disorders and administration site conditions  |                         |  |  |

|                             |               |  |  |
|-----------------------------|---------------|--|--|
| Asthenia                    |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Chest Discomfort            |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Chest Pain                  |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Chills                      |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Fatigue                     |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Feeling Cold                |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Gait Disturbance            |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Irritability                |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Oedema Peripheral           |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Pyrexia                     |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Sense of Oppression         |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Immune system disorders     |               |  |  |
| Seasonal Allergy            |               |  |  |

|  |                     |  |  |
|--|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Reproductive system and breast disorders         |                     |  |  |
| Dysmenorrhoea                                    |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Hypomenorrhoea                                   |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Respiratory, thoracic and mediastinal disorders  |                     |  |  |
| Bronchitis Chronic                               |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Cough  |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Dyspnoea   |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Epistaxis  |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Hyperventilation                                 |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Nasal Congestion                                 |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Rhinitis Allergic                                |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>1 |  |  |
| Oropharyngeal Pain                               |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  |  |  |
| Rhinorrhoea                                      |                     |  |  |

|                                 |               |  |  |
|---------------------------------|---------------|--|--|
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Sinus Congestion                |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Psychiatric disorders           |               |  |  |
| Aggression                      |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Anxiety                         |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Depression                      |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Disturbance in Social Behaviour |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Dysphoria                       |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Insomnia                        |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Libido Decreased                |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Nervousness                     |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Stress                          |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |
| Suicidal Ideation               |               |  |  |
| subjects affected / exposed     | 0 / 2 (0.00%) |  |  |
| occurrences (all)               | 0             |  |  |

|  |               |  |  |
|--|---------------|--|--|
| Investigations                                 |               |  |  |
| Alanine Aminotransferase Increased             |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Aspartate Aminotransferase Increased           |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Blood Pressure Increased                       |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Weight Decreased                               |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Weight Increased                               |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Injury, poisoning and procedural complications |               |  |  |
| Contusion                                      |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Excoriation                                    |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Fall   |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Head Injury                                    |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Joint Injury                                   |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Laceration                                     |               |  |  |
| subjects affected / exposed                    | 0 / 2 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Ligament Sprain                                |               |  |  |

|  |   |  |  |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Skin Laceration</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Thermal Burn</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Wound</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 2 (0.00%)</p> <p>0</p> <p>0 / 2 (0.00%)</p> <p>0</p> <p>0 / 2 (0.00%)</p> <p>0</p> <p>0 / 2 (0.00%)</p> <p>0</p>                               |  |  |
| <p>Cardiac disorders</p> <p>Cardiac Discomfort</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Palpitations</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 2 (0.00%)</p> <p>0</p> <p>0 / 2 (0.00%)</p> <p>0</p>   |  |  |
| <p>Nervous system disorders</p> <p>Ageusia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Agnosia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Amnesia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Ataxia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Balance Disorder</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Convulsion</p> | <p>0 / 2 (0.00%)</p> <p>0</p> <p>0 / 2 (0.00%)</p> <p>0</p> <p>0 / 2 (0.00%)</p> <p>0</p> <p>0 / 2 (0.00%)</p> <p>0</p> <p>0 / 2 (0.00%)</p> <p>0</p> |  |  |



|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 2 (50.00%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Dizziness                   |                 |  |  |
| subjects affected / exposed | 2 / 2 (100.00%) |  |  |
| occurrences (all)           | 2               |  |  |
| Disturbance in Attention    |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Facial Palsy                |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Head Discomfort             |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Headache                    |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Hypoaesthesia               |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Hypotonia                   |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Lethargy                    |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Memory Impairment           |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Migraine                    |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Nystagmus                   |                 |  |  |
| subjects affected / exposed | 0 / 2 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Paraesthesia                |                 |  |  |

|                                      |               |  |  |
|--------------------------------------|---------------|--|--|
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Poor Quality Sleep                   |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Postictal State                      |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Sedation                             |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Simple Partial Seizures              |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Somnolence                           |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Tension Headache                     |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Tremor                               |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Blood and lymphatic system disorders |               |  |  |
| Anaemia                              |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Ear and labyrinth disorders          |               |  |  |
| Ear Pain                             |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Vertigo                              |               |  |  |
| subjects affected / exposed          | 0 / 2 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Eye disorders                        |               |  |  |

|                             |               |  |  |
|-----------------------------|---------------|--|--|
| Cataract                    |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Diplopia                    |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Eye Movement Disorder       |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Lacrimation Increased       |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Vision Blurred              |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Visual Acuity Reduced       |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Visual Impairment           |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Gastrointestinal disorders  |               |  |  |
| Abdominal Pain              |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Abdominal Pain Lower        |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Abdominal Pain Upper        |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Aphthous Stomatitis         |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Constipation                |               |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Diarrhoea                              |                |  |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Duodenitis                             |                |  |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Dyspepsia                              |                |  |  |
| subjects affected / exposed            | 1 / 2 (50.00%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Gastric Ulcer                          |                |  |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Gastritis                              |                |  |  |
| subjects affected / exposed            | 1 / 2 (50.00%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Gastrooesophageal Reflux Disease       |                |  |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Nausea                                 |                |  |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Periodontitis                          |                |  |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Rectal Haemorrhage                     |                |  |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Toothache                              |                |  |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Vomiting                               |                |  |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Skin and subcutaneous tissue disorders |                |  |  |

|   |                             |               |  |  |
|---|-----------------------------|---------------|--|--|
| Alopecia  | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
| Decubitus Ulcer                                 | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
| Dermal Cyst                                     | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
| Eczema  | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
| Hypoaesthesia Facial                            | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
| Rash  | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
| Pruritus  | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
| Urticaria                                       | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
| Renal and urinary disorders                     |                             |               |  |  |
|   | Dysuria                     |               |  |  |
|   | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
|   | Polyuria                    |               |  |  |
|   | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
|   | Urinary Tract Pain          |               |  |  |
|   | subjects affected / exposed | 0 / 2 (0.00%) |  |  |
|   | occurrences (all)           | 0             |  |  |
| Musculoskeletal and connective tissue disorders |                             |               |  |  |

|                             |               |  |  |
|-----------------------------|---------------|--|--|
| Arthralgia                  |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Back Pain                   |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Bone Pain                   |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Flank Pain                  |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Muscle Spasms               |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Musculoskeletal Pain        |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Musculoskeletal Stiffness   |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Myalgia                     |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Neck Pain                   |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Pain in Extremity           |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Tenosynovitis               |               |  |  |
| subjects affected / exposed | 0 / 2 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Infections and infestations |               |  |  |
| Bronchitis                  |               |  |  |

|                                   |                |  |  |
|-----------------------------------|----------------|--|--|
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Candidiasis                       |                |  |  |
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Ear Infection                     |                |  |  |
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Gastroenteritis                   |                |  |  |
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Gastroenteritis Viral             |                |  |  |
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Influenza                         |                |  |  |
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Laryngitis                        |                |  |  |
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Nasopharyngitis                   |                |  |  |
| subjects affected / exposed       | 1 / 2 (50.00%) |  |  |
| occurrences (all)                 | 5              |  |  |
| Pharyngitis                       |                |  |  |
| subjects affected / exposed       | 1 / 2 (50.00%) |  |  |
| occurrences (all)                 | 2              |  |  |
| Sinusitis                         |                |  |  |
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Tonsillitis                       |                |  |  |
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Upper Respiratory Tract Infection |                |  |  |
| subjects affected / exposed       | 0 / 2 (0.00%)  |  |  |
| occurrences (all)                 | 0              |  |  |
| Urinary Tract Infection           |                |  |  |

|                                    |               |  |  |
|------------------------------------|---------------|--|--|
| subjects affected / exposed        | 0 / 2 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Viral Infection                    |               |  |  |
| subjects affected / exposed        | 0 / 2 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Metabolism and nutrition disorders |               |  |  |
| Appetite Disorder                  |               |  |  |
| subjects affected / exposed        | 0 / 2 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Decreased Appetite                 |               |  |  |
| subjects affected / exposed        | 0 / 2 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Hypercholesterolaemia              |               |  |  |
| subjects affected / exposed        | 0 / 2 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Hyponatraemia                      |               |  |  |
| subjects affected / exposed        | 0 / 2 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Polydipsia                         |               |  |  |
| subjects affected / exposed        | 0 / 2 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 02 February 2007  | Decreased the required stable duration of concomitant antiepileptic drug (AED) dosage to be for at least 1 month prior to enrollment; increased monitoring frequency for the occurrence of withdrawal symptoms, and updated the time and events schedule to reflect changes in study procedures  |
| 04 September 2007 | It clarified the endpoint for registration in the United States and the Rest of the World, evaluation and measurement of QTc interval using Fridericia's correction (QTcF), and added additional cardiac-related outcomes  |
| 02 November 2007  | It included appropriate corrections to maintain consistency between the synopsis and report body and updates according to amendment INT-2  |
| 08 September 2008 | It included increase in the maximum allowed dose in the open-label extension phase from 800 mg per day to 1200 mg per day, replacement of RWJ-333369 by carisbamate to promote name recognition in sections on open-label extension, and added rationales for permitting slow study drug tapering schedule and dosage strengths of the tablets available in the open-label extension phase |
| 14 October 2009   | It included additional withdrawal criteria regarding potential symptoms of Drug Rash with Eosinophilia and Systemic Signs  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported