



## Clinical trial results:

### A Multicenter 26-Week Extension Study to Evaluate the Safety and Clinical Effects of Prolonged Exposure to 1 and 2 mg Doses of EVP-6124, an Alpha-7 Nicotinic Acetylcholine Receptor Agonist, as an Adjunctive Pro-cognitive Treatment in Subjects with Schizophrenia on Chronic Stable Atypical Antipsychotic Therapy

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2012-003228-19  |
| Trial protocol           | ES DE IT GB PL  |
| Global end of trial date | 16 October 2015 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 31 October 2016 |
| First version publication date | 31 October 2016 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | EVP-6124-017 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |                    |
|------------------------------------|--------------------|
| ISRCTN number                      | -                  |
| ClinicalTrials.gov id (NCT number) | -                  |
| WHO universal trial number (UTN)   | -                  |
| Other trial identifiers            | IND Number: 076939 |

Notes:

#### Sponsors

|                              |                                                                                               |
|------------------------------|-----------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Forum Pharmaceuticals, Inc.                                                                   |
| Sponsor organisation address | 500 Arsenal Street, Watertown, MA, United States, 02472                                       |
| Public contact               | Regulatory Project Manager, INC Research, +44 1276481000, SM_Regaffairs_eu_ap@incresearch.com |
| Scientific contact           | Regulatory Project Manager, INC Research, +44 1276481000, SM_Regaffairs_eu_ap@incresearch.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                       | 12 May 2016     |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 16 October 2015 |
| Was the trial ended prematurely?                     | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

To assess the long-term safety of 1 and 2 mg doses of EVP-6124 tablets administered once daily for up to 52 weeks in subjects who received EVP-6124 in both the pivotal and extension studies and up to 26 weeks in subjects who were randomized from placebo to EVP-6124 upon entry into this extension study.

Protection of trial subjects:

There were no specific measures as the only 'invasive' measures were blood sample analyses.

Background therapy:

Patients were enrolled into the antecedent studies (015 and 016) that were stably treated with atypical anti-psychotic agents. These are the standard treatment of choice for this patient population. Only the anti-psychotic clozapine was excluded. This was for two reasons: clozapine treated patients are uniquely 'sicker' as it remains a second or third line treatment choice and clozapine has safety concerns which require special monitoring procedures that would more difficult to incorporate into the studies.

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 13 June 2013 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Poland: 23             |
| Country: Number of subjects enrolled | Spain: 26              |
| Country: Number of subjects enrolled | United Kingdom: 5      |
| Country: Number of subjects enrolled | Germany: 14            |
| Country: Number of subjects enrolled | Italy: 11              |
| Country: Number of subjects enrolled | Argentina: 37          |
| Country: Number of subjects enrolled | Australia: 2           |
| Country: Number of subjects enrolled | Canada: 26             |
| Country: Number of subjects enrolled | Colombia: 29           |
| Country: Number of subjects enrolled | Mexico: 25             |
| Country: Number of subjects enrolled | Romania: 30            |
| Country: Number of subjects enrolled | Russian Federation: 60 |
| Country: Number of subjects enrolled | Serbia: 7              |
| Country: Number of subjects enrolled | Singapore: 2           |
| Country: Number of subjects enrolled | Ukraine: 127           |
| Country: Number of subjects enrolled | United States: 403     |

|                                    |     |
|------------------------------------|-----|
| Worldwide total number of subjects | 827 |
| EEA total number of subjects       | 109 |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 827 |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects who completed double-blind treatment (ie, completion of the Day 182 Visit) in Studies EVP-6124-015 or EVP-6124-016 and who fulfilled all inclusion/exclusion criteria for this extension study were eligible for enrollment.

### Pre-assignment period milestones

|                              |     |
|------------------------------|-----|
| Number of subjects started   | 827 |
| Number of subjects completed | 827 |

### Period 1

|                              |                                 |
|------------------------------|---------------------------------|
| Period 1 title               | Overall period (overall period) |
| Is this the baseline period? | Yes                             |
| Allocation method            | Randomised - controlled         |
| Blinding used                | Double blind                    |
| Roles blinded                | Subject, Investigator           |

### Arms

|                              |                |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes            |
| <b>Arm title</b>             | EVP-6124, 1 mg |

Arm description:

Subjects who received EVP-6124 during the previous study (EVP-6124-015 or EVP-6124-016) will remain on the same dose. Subjects who received placebo during the pivotal study (EVP-6124-015 or EVP-6124-016) will be randomized (1:1 ratio) to once daily EVP-6124 1 or 2 mg tablets for up to 26 weeks (Days 1-182).

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Encenicline  |
| Investigational medicinal product code | EVP-6124     |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Throughout the study (Days 1-182), all subjects will be instructed to take 1 tablet of study medication once daily, preferably at the same time (between 8 to 10 AM if feasible) every morning, with an adequate amount of water with or without food (after morning meal is preferred).

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | EVP-6124, 2 mg |
|------------------|----------------|

Arm description:

Subjects who received EVP-6124 during the previous study (EVP-6124-015 or EVP-6124-016) will remain on the same dose. Subjects who received placebo during the pivotal study (EVP-6124-015 or EVP-6124-016) will be randomized (1:1 ratio) to once daily EVP-6124 1 or 2 mg tablets for up to 26 weeks (Days 1-182).

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Encenicline  |
| Investigational medicinal product code | EVP-6124     |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

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**Dosage and administration details:**

Throughout the study (Days 1-182), all subjects will be instructed to take 1 tablet of study medication once daily, preferably at the same time (between 8 to 10 AM if feasible) every morning, with an adequate amount of water with or without food (after morning meal is preferred).

| <b>Number of subjects in period 1</b> | <b>EVP-6124, 1 mg</b> | <b>EVP-6124, 2 mg</b> |
|---------------------------------------|-----------------------|-----------------------|
| Started                               | 428                   | 399                   |
| Completed                             | 248                   | 223                   |
| Not completed                         | 180                   | 176                   |
| Physician decision                    | 1                     | 1                     |
| Consent withdrawn by subject          | 14                    | 12                    |
| Adverse event, non-fatal              | 13                    | 17                    |
| Medication Prohibited by Protocol     | 2                     | 1                     |
| Subject Incarceration                 | 2                     | 1                     |
| Substance Abuse                       | -                     | 1                     |
| Sponsor Decision                      | 136                   | 129                   |
| Lost to follow-up                     | 9                     | 10                    |
| Protocol deviation                    | 3                     | 4                     |

## Baseline characteristics

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | EVP-6124, 1 mg |
|-----------------------|----------------|

Reporting group description:

Subjects who received EVP-6124 during the previous study (EVP-6124-015 or EVP-6124-016) will remain on the same dose. Subjects who received placebo during the pivotal study (EVP-6124-015 or EVP-6124-016) will be randomized (1:1 ratio) to once daily EVP-6124 1 or 2 mg tablets for up to 26 weeks (Days 1-182).

|                       |                |
|-----------------------|----------------|
| Reporting group title | EVP-6124, 2 mg |
|-----------------------|----------------|

Reporting group description:

Subjects who received EVP-6124 during the previous study (EVP-6124-015 or EVP-6124-016) will remain on the same dose. Subjects who received placebo during the pivotal study (EVP-6124-015 or EVP-6124-016) will be randomized (1:1 ratio) to once daily EVP-6124 1 or 2 mg tablets for up to 26 weeks (Days 1-182).

| Reporting group values                | EVP-6124, 1 mg | EVP-6124, 2 mg | Total |
|---------------------------------------|----------------|----------------|-------|
| Number of subjects                    | 428            | 399            | 827   |
| Age categorical<br>Units: Subjects    |                |                |       |
| Adults (18-64 years)                  | 428            | 399            | 827   |
| Age continuous<br>Units: years        |                |                |       |
| arithmetic mean                       | 37.4           | 37             |       |
| full range (min-max)                  | 18 to 51       | 18 to 51       | -     |
| Gender categorical<br>Units: Subjects |                |                |       |
| Female                                | 151            | 138            | 289   |
| Male                                  | 277            | 261            | 538   |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                      |                |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                | EVP-6124, 1 mg |
| Reporting group description:<br>Subjects who received EVP-6124 during the previous study (EVP-6124-015 or EVP-6124-016) will remain on the same dose. Subjects who received placebo during the pivotal study (EVP-6124-015 or EVP-6124-016) will be randomized (1:1 ratio) to once daily EVP-6124 1 or 2 mg tablets for up to 26 weeks (Days 1-182). |                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                | EVP-6124, 2 mg |
| Reporting group description:<br>Subjects who received EVP-6124 during the previous study (EVP-6124-015 or EVP-6124-016) will remain on the same dose. Subjects who received placebo during the pivotal study (EVP-6124-015 or EVP-6124-016) will be randomized (1:1 ratio) to once daily EVP-6124 1 or 2 mg tablets for up to 26 weeks (Days 1-182). |                |

### Primary: Treatment emergent adverse events (TEAEs)

|                                                                                                                                                                                                                                                                                       |                                                          |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                       | Treatment emergent adverse events (TEAEs) <sup>[1]</sup> |
| End point description:                                                                                                                                                                                                                                                                |                                                          |
| End point type                                                                                                                                                                                                                                                                        | Primary                                                  |
| End point timeframe:<br>Throughout the study                                                                                                                                                                                                                                          |                                                          |
| Notes:<br>[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.<br>Justification: This was a safety extension study, so there were no pre-defined statistical analysis. |                                                          |

| End point values               | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|--------------------------------|-----------------|-----------------|--|--|
| Subject group type             | Reporting group | Reporting group |  |  |
| Number of subjects analysed    | 428             | 399             |  |  |
| Units: Subjects with any TEAEs | 164             | 149             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Columbia-Suicide Severity Rating Scale (C-SSRS) (Day 182)

|                                                                           |                                                                          |
|---------------------------------------------------------------------------|--------------------------------------------------------------------------|
| End point title                                                           | Columbia-Suicide Severity Rating Scale (C-SSRS) (Day 182) <sup>[2]</sup> |
| End point description:                                                    |                                                                          |
| End point type                                                            | Primary                                                                  |
| End point timeframe:<br>On Days 14, 28, 56, 84, 112, 140, and 182, or ET. |                                                                          |

Notes:

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

Justification: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                              | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|-----------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                            | Reporting group | Reporting group |  |  |
| Number of subjects analysed                   | 428             | 399             |  |  |
| Units: Subjects who had any suicidal ideation | 4               | 1               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Calgary Depression Scale for Schizophrenia (CDSS) (change from baseline)

|                 |                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------|
| End point title | Calgary Depression Scale for Schizophrenia (CDSS) (change from baseline) <sup>[3]</sup> |
|-----------------|-----------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

The CDSS will be completed at Day 182 or ET. The CDSS was performed at the final study visit (Day 182) for the previous study (EVP-6124-015 or EVP-6124-016), and this value will serve as the baseline assessment.

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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg   | EVP-6124, 2 mg  |  |  |
|----------------------------------------|------------------|-----------------|--|--|
| Subject group type                     | Reporting group  | Reporting group |  |  |
| Number of subjects analysed            | 428              | 399             |  |  |
| Units: n/a                             |                  |                 |  |  |
| arithmetic mean (full range (min-max)) | -0.1 (-12 to 10) | 0 (-9 to 9)     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Simpson-Angus Scale (SAS) (change from baseline)

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Simpson-Angus Scale (SAS) (change from baseline) <sup>[4]</sup> |
|-----------------|-----------------------------------------------------------------|

End point description:

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

End point timeframe:

On Days 56, 112, and 182, or ET.



Notes:

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

Justification: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: n/a                             |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 0 (-4 to 4)     | 0 (-4 to 3)     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Heart rate (change from baseline)

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Heart rate (change from baseline) <sup>[5]</sup> |
|-----------------|--------------------------------------------------|

End point description:

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

End point timeframe:

On Days 28, 56, 112, and 182, or ET.

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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: beats/min                       |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 2.1 (-42 to 43) | 0.4 (-39 to 37) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: QT duration (change from baseline)

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | QT duration (change from baseline) <sup>[6]</sup> |
|-----------------|---------------------------------------------------|

End point description:

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

End point timeframe:

On Days 28, 56, 112, and 182, or ET.

Notes:

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

Justification: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg   | EVP-6124, 2 mg   |  |  |
|----------------------------------------|------------------|------------------|--|--|
| Subject group type                     | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed            | 428              | 399              |  |  |
| Units: msec                            |                  |                  |  |  |
| arithmetic mean (full range (min-max)) | -3.5 (-87 to 83) | -1.2 (-82 to 88) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: QTcF - Fridericia's Correction (change from baseline)

|                 |                                                                      |
|-----------------|----------------------------------------------------------------------|
| End point title | QTcF - Fridericia's Correction (change from baseline) <sup>[7]</sup> |
|-----------------|----------------------------------------------------------------------|

End point description:

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

End point timeframe:

On Days 28, 56, 112, and 182, or ET.

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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg   |  |  |
|----------------------------------------|-----------------|------------------|--|--|
| Subject group type                     | Reporting group | Reporting group  |  |  |
| Number of subjects analysed            | 428             | 399              |  |  |
| Units: msec                            |                 |                  |  |  |
| arithmetic mean (full range (min-max)) | 0 (-49 to 50)   | -0.8 (-43 to 61) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: QRS Duration (change from baseline)

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | QRS Duration (change from baseline) <sup>[8]</sup> |
|-----------------|----------------------------------------------------|

End point description:

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

End point timeframe:

On Days 28, 56, 112, and 182, or ET.

Notes:

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

Justification: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: msec                            |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 0.1 (-23 to 22) | 0.2 (-21 to 19) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: PR Duration (change from baseline)

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | PR Duration (change from baseline) <sup>[9]</sup> |
|-----------------|---------------------------------------------------|

End point description:

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

End point timeframe:

On Days 28, 56, 112, and 182, or ET.

Notes:

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

Justification: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: msec                            |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | -2 (-65 to 73)  | 0.5 (-26 to 51) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: RR duration (change from baseline)

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | RR duration (change from baseline) <sup>[10]</sup> |
|-----------------|----------------------------------------------------|

End point description:

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

End point timeframe:

On Days 28, 56, 112, and 182, or ET.

Notes:

[10] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg      | EVP-6124, 2 mg   |  |  |
|----------------------------------------|---------------------|------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group  |  |  |
| Number of subjects analysed            | 428                 | 399              |  |  |
| Units: msec                            |                     |                  |  |  |
| arithmetic mean (full range (min-max)) | -22.7 (-472 to 468) | -2 (-567 to 346) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Basophils (change from baseline)

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Basophils (change from baseline) <sup>[11]</sup> |
|-----------------|--------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[11] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg       | EVP-6124, 2 mg    |  |  |
|----------------------------------------|----------------------|-------------------|--|--|
| Subject group type                     | Reporting group      | Reporting group   |  |  |
| Number of subjects analysed            | 428                  | 399               |  |  |
| Units: 10 <sup>9</sup> /L              |                      |                   |  |  |
| arithmetic mean (full range (min-max)) | 0.001 (-0.09 to 0.1) | 0 (-0.05 to 0.08) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Eosinophils (change from baseline)

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | Eosinophils (change from baseline) <sup>[12]</sup> |
|-----------------|----------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[12] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg        | EVP-6124, 2 mg         |  |  |
|----------------------------------------|-----------------------|------------------------|--|--|
| Subject group type                     | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed            | 428                   | 399                    |  |  |
| Units: 10 <sup>9</sup> /L              |                       |                        |  |  |
| arithmetic mean (full range (min-max)) | -0.005 (-0.44 to 0.4) | -0.008 (-0.63 to 0.56) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Erythrocytes (change from baseline)

|                 |                                                     |
|-----------------|-----------------------------------------------------|
| End point title | Erythrocytes (change from baseline) <sup>[13]</sup> |
|-----------------|-----------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[13] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg         | EVP-6124, 2 mg        |  |  |
|----------------------------------------|------------------------|-----------------------|--|--|
| Subject group type                     | Reporting group        | Reporting group       |  |  |
| Number of subjects analysed            | 428                    | 399                   |  |  |
| Units: 10 <sup>12</sup> /L             |                        |                       |  |  |
| arithmetic mean (full range (min-max)) | -0.009 (-1.03 to 1.79) | 0.018 (-1.02 to 2.46) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Hematocrit (change from baseline)

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | Hematocrit (change from baseline) <sup>[14]</sup> |
|-----------------|---------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[14] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg      | EVP-6124, 2 mg       |  |  |
|----------------------------------------|---------------------|----------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group      |  |  |
| Number of subjects analysed            | 428                 | 399                  |  |  |
| Units: percent                         |                     |                      |  |  |
| arithmetic mean (full range (min-max)) | 0.23 (-7.8 to 15.4) | 0.23 (-10.5 to 12.4) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Hemoglobin (change from baseline)

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | Hemoglobin (change from baseline) <sup>[15]</sup> |
|-----------------|---------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[15] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg   | EVP-6124, 2 mg  |  |  |
|----------------------------------------|------------------|-----------------|--|--|
| Subject group type                     | Reporting group  | Reporting group |  |  |
| Number of subjects analysed            | 428              | 399             |  |  |
| Units: g/dL                            |                  |                 |  |  |
| arithmetic mean (full range (min-max)) | 0.01 (-3 to 5.2) | 0 (-4.1 to 3.2) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Leukocytes (change from baseline)

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | Leukocytes (change from baseline) <sup>[16]</sup> |
|-----------------|---------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[16] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg        | EVP-6124, 2 mg        |  |  |
|----------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                     | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed            | 428                   | 399                   |  |  |
| Units: 10 <sup>9</sup> /L              |                       |                       |  |  |
| arithmetic mean (full range (min-max)) | 0.023 (-5.66 to 6.84) | -0.094 (-5.3 to 5.75) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Lymphocytes (change from baseline)

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | Lymphocytes (change from baseline) <sup>[17]</sup> |
|-----------------|----------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[17] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg      | EVP-6124, 2 mg        |  |  |
|----------------------------------------|---------------------|-----------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed            | 428                 | 399                   |  |  |
| Units: 10 <sup>9</sup> /L              |                     |                       |  |  |
| arithmetic mean (full range (min-max)) | 0.027 (-1.5 to 2.1) | 0.004 (-1.34 to 2.16) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Monocytes (change from baseline)

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Monocytes (change from baseline) <sup>[18]</sup> |
|-----------------|--------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[18] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg         | EVP-6124, 2 mg        |  |  |
|----------------------------------------|------------------------|-----------------------|--|--|
| Subject group type                     | Reporting group        | Reporting group       |  |  |
| Number of subjects analysed            | 428                    | 399                   |  |  |
| Units: 10 <sup>9</sup> /L              |                        |                       |  |  |
| arithmetic mean (full range (min-max)) | -0.021 (-0.78 to 0.66) | -0.018 (-0.6 to 0.41) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Neutrophils (change from baseline)

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | Neutrophils (change from baseline) <sup>[19]</sup> |
|-----------------|----------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[19] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg      | EVP-6124, 2 mg         |  |  |
|----------------------------------------|---------------------|------------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed            | 428                 | 399                    |  |  |
| Units: 10 <sup>9</sup> /L              |                     |                        |  |  |
| arithmetic mean (full range (min-max)) | 0.01 (-6.6 to 6.64) | -0.112 (-4.75 to 4.42) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Platelets (change from baseline)

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Platelets (change from baseline) <sup>[20]</sup> |
|-----------------|--------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.



Notes:

[20] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg    | EVP-6124, 2 mg    |  |  |
|----------------------------------------|-------------------|-------------------|--|--|
| Subject group type                     | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed            | 428               | 399               |  |  |
| Units: 10 <sup>9</sup> /L              |                   |                   |  |  |
| arithmetic mean (full range (min-max)) | 0.6 (-126 to 225) | 0.2 (-145 to 162) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Alanine Aminotransferase (change from baseline)

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Alanine Aminotransferase (change from baseline) <sup>[21]</sup> |
|-----------------|-----------------------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[21] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg    | EVP-6124, 2 mg   |  |  |
|----------------------------------------|-------------------|------------------|--|--|
| Subject group type                     | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed            | 428               | 399              |  |  |
| Units: IU/L                            |                   |                  |  |  |
| arithmetic mean (full range (min-max)) | -0.4 (-67 to 112) | 1.2 (-87 to 234) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Albumin (change from baseline)

|                 |                                                |
|-----------------|------------------------------------------------|
| End point title | Albumin (change from baseline) <sup>[22]</sup> |
|-----------------|------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[22] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg      | EVP-6124, 2 mg      |  |  |
|----------------------------------------|---------------------|---------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed            | 428                 | 399                 |  |  |
| Units: g/dL                            |                     |                     |  |  |
| arithmetic mean (full range (min-max)) | -0.03 (-0.9 to 1.1) | -0.05 (-0.9 to 0.7) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Alkaline Phosphatase (change from baseline)

|                 |                                                             |
|-----------------|-------------------------------------------------------------|
| End point title | Alkaline Phosphatase (change from baseline) <sup>[23]</sup> |
|-----------------|-------------------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[23] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: IU/L                            |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | -1 (-51 to 85)  | 0.5 (-91 to 57) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Aspartate Aminotransferase (change from baseline)

|                 |                                                                   |
|-----------------|-------------------------------------------------------------------|
| End point title | Aspartate Aminotransferase (change from baseline) <sup>[24]</sup> |
|-----------------|-------------------------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[24] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg   | EVP-6124, 2 mg  |  |  |
|----------------------------------------|------------------|-----------------|--|--|
| Subject group type                     | Reporting group  | Reporting group |  |  |
| Number of subjects analysed            | 428              | 399             |  |  |
| Units: IU/L                            |                  |                 |  |  |
| arithmetic mean (full range (min-max)) | 0.5 (-56 to 217) | 1 (-74 to 111)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Bicarbonate (change from baseline)

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | Bicarbonate (change from baseline) <sup>[25]</sup> |
|-----------------|----------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[25] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: mEq/L                           |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | -0.5 (-9 to 8)  | -0.5 (-7 to 6)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Bilirubin (change from baseline)

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Bilirubin (change from baseline) <sup>[26]</sup> |
|-----------------|--------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[26] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg     | EVP-6124, 2 mg      |  |  |
|----------------------------------------|--------------------|---------------------|--|--|
| Subject group type                     | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed            | 428                | 399                 |  |  |
| Units: mg/dL                           |                    |                     |  |  |
| arithmetic mean (full range (min-max)) | 0.02 (-0.5 to 2.3) | -0.01 (-1.1 to 1.1) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Blood Urea Nitrogen (change from baseline)

|                 |                                                            |
|-----------------|------------------------------------------------------------|
| End point title | Blood Urea Nitrogen (change from baseline) <sup>[27]</sup> |
|-----------------|------------------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[27] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: mg/dL                           |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 0 (-8 to 25)    | -0.4 (-16 to 9) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Calcium (change from baseline)

|                 |                                                |
|-----------------|------------------------------------------------|
| End point title | Calcium (change from baseline) <sup>[28]</sup> |
|-----------------|------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[28] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg      | EVP-6124, 2 mg     |  |  |
|----------------------------------------|---------------------|--------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed            | 428                 | 399                |  |  |
| Units: mg/dL                           |                     |                    |  |  |
| arithmetic mean (full range (min-max)) | -0.01 (-1.2 to 1.7) | 0.01 (-1.2 to 1.4) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Chloride (change from baseline)

|                 |                                                 |
|-----------------|-------------------------------------------------|
| End point title | Chloride (change from baseline) <sup>[29]</sup> |
|-----------------|-------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[29] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: mEq/L                           |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | -0.2 (-17 to 8) | -0.1 (-10 to 6) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Creatine Kinase (change from baseline)

|                 |                                                        |
|-----------------|--------------------------------------------------------|
| End point title | Creatine Kinase (change from baseline) <sup>[30]</sup> |
|-----------------|--------------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[30] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg      | EVP-6124, 2 mg      |  |  |
|----------------------------------------|---------------------|---------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed            | 428                 | 399                 |  |  |
| Units: IU/L                            |                     |                     |  |  |
| arithmetic mean (full range (min-max)) | 29.9 (-953 to 4605) | 8.9 (-1359 to 4853) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Creatinine (change from baseline)

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | Creatinine (change from baseline) <sup>[31]</sup> |
|-----------------|---------------------------------------------------|

End point description:

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

End point timeframe:

Visits 1, 2, 3, 5 and 7

Notes:

[31] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg        | EVP-6124, 2 mg        |  |  |
|----------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                     | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed            | 428                   | 399                   |  |  |
| Units: mg/dL                           |                       |                       |  |  |
| arithmetic mean (full range (min-max)) | 0.016 (-0.46 to 1.51) | 0.003 (-0.47 to 0.39) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Gamma Glutamyl Transferase (change from baseline)

|                 |                                                                   |
|-----------------|-------------------------------------------------------------------|
| End point title | Gamma Glutamyl Transferase (change from baseline) <sup>[32]</sup> |
|-----------------|-------------------------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[32] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg    | EVP-6124, 2 mg   |  |  |
|----------------------------------------|-------------------|------------------|--|--|
| Subject group type                     | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed            | 428               | 399              |  |  |
| Units: IU/L                            |                   |                  |  |  |
| arithmetic mean (full range (min-max)) | 0.1 (-109 to 167) | 1.1 (-229 to 78) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Glomerular Filtration Rate (change from baseline)

|                 |                                                                   |
|-----------------|-------------------------------------------------------------------|
| End point title | Glomerular Filtration Rate (change from baseline) <sup>[33]</sup> |
|-----------------|-------------------------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[33] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: mL/min/1.73m <sup>2</sup>       |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | -0.2 (-32 to 5) | 0 (-5 to 5)     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Glucose (change from baseline)

|                 |                                                |
|-----------------|------------------------------------------------|
| End point title | Glucose (change from baseline) <sup>[34]</sup> |
|-----------------|------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[34] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg     | EVP-6124, 2 mg    |  |  |
|----------------------------------------|--------------------|-------------------|--|--|
| Subject group type                     | Reporting group    | Reporting group   |  |  |
| Number of subjects analysed            | 428                | 399               |  |  |
| Units: mg/dL                           |                    |                   |  |  |
| arithmetic mean (full range (min-max)) | -1.3 (-215 to 175) | 3.3 (-142 to 208) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Magnesium (change from baseline)

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Magnesium (change from baseline) <sup>[35]</sup> |
|-----------------|--------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[35] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg      |  |  |
|----------------------------------------|-----------------|---------------------|--|--|
| Subject group type                     | Reporting group | Reporting group     |  |  |
| Number of subjects analysed            | 428             | 399                 |  |  |
| Units: mg/dL                           |                 |                     |  |  |
| arithmetic mean (full range (min-max)) | 0 (-0.5 to 1)   | -0.01 (-0.5 to 0.4) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Phosphate (change from baseline)

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Phosphate (change from baseline) <sup>[36]</sup> |
|-----------------|--------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.



Notes:

[36] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg    | EVP-6124, 2 mg      |  |  |
|----------------------------------------|-------------------|---------------------|--|--|
| Subject group type                     | Reporting group   | Reporting group     |  |  |
| Number of subjects analysed            | 428               | 399                 |  |  |
| Units: mg/dL                           |                   |                     |  |  |
| arithmetic mean (full range (min-max)) | -0.02 (-2 to 5.8) | -0.03 (-1.9 to 2.2) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Potassium (change from baseline)

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Potassium (change from baseline) <sup>[37]</sup> |
|-----------------|--------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[37] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg     | EVP-6124, 2 mg     |  |  |
|----------------------------------------|--------------------|--------------------|--|--|
| Subject group type                     | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed            | 428                | 399                |  |  |
| Units: mEq/L                           |                    |                    |  |  |
| arithmetic mean (full range (min-max)) | 0.02 (-1.6 to 1.7) | 0.08 (-1.1 to 1.2) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Prolactin (change from baseline)

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Prolactin (change from baseline) <sup>[38]</sup> |
|-----------------|--------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[38] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg       | EVP-6124, 2 mg        |  |  |
|----------------------------------------|----------------------|-----------------------|--|--|
| Subject group type                     | Reporting group      | Reporting group       |  |  |
| Number of subjects analysed            | 428                  | 399                   |  |  |
| Units: ug/L                            |                      |                       |  |  |
| arithmetic mean (full range (min-max)) | 1.88 (-149.1 to 175) | -2.25 (-88.9 to 74.8) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Protein (change from baseline)

|                 |                                                |
|-----------------|------------------------------------------------|
| End point title | Protein (change from baseline) <sup>[39]</sup> |
|-----------------|------------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[39] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg      | EVP-6124, 2 mg      |  |  |
|----------------------------------------|---------------------|---------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed            | 428                 | 399                 |  |  |
| Units: g/dL                            |                     |                     |  |  |
| arithmetic mean (full range (min-max)) | -0.05 (-2.1 to 1.2) | -0.04 (-1.7 to 1.1) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Sodium (change from baseline)

|                 |                                               |
|-----------------|-----------------------------------------------|
| End point title | Sodium (change from baseline) <sup>[40]</sup> |
|-----------------|-----------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[40] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: mEq/L                           |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 0.5 (-7 to 11)  | 0.6 (-7 to 10)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Urate (change from baseline)

|                 |                                              |
|-----------------|----------------------------------------------|
| End point title | Urate (change from baseline) <sup>[41]</sup> |
|-----------------|----------------------------------------------|

End point description:

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

End point timeframe:

These non-fasting laboratory tests will be performed on Days 28, 56, 112, and 182, or ET.

Notes:

[41] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg     | EVP-6124, 2 mg    |  |  |
|----------------------------------------|--------------------|-------------------|--|--|
| Subject group type                     | Reporting group    | Reporting group   |  |  |
| Number of subjects analysed            | 428                | 399               |  |  |
| Units: mg/dL                           |                    |                   |  |  |
| arithmetic mean (full range (min-max)) | 0.05 (-4.8 to 4.9) | -0.04 (-4.8 to 3) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Systolic Blood Pressure (change from baseline)

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Systolic Blood Pressure (change from baseline) <sup>[42]</sup> |
|-----------------|----------------------------------------------------------------|

End point description:

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

End point timeframe:

At all study visits (except Day 14 telephone call).

Notes:

[42] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: mmHg                            |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 0.4 (-40 to 41) | 0.2 (-31 to 32) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Diastolic Blood Pressure (change from baseline)

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Diastolic Blood Pressure (change from baseline) <sup>[43]</sup> |
|-----------------|-----------------------------------------------------------------|

End point description:

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

End point timeframe:

At all study visits (except Day 14 telephone call).

Notes:

[43] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: mmHg                            |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 0.1 (-32 to 42) | 0.7 (-30 to 33) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Pulse Rate (change from baseline)

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | Pulse Rate (change from baseline) <sup>[44]</sup> |
|-----------------|---------------------------------------------------|

End point description:

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

End point timeframe:

At all study visits (except Day 14 telephone call).

Notes:

[44] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: beats/min                       |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 2.3 (-33 to 46) | 0.9 (-29 to 27) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Respiratory Rate (change from baseline)

|                 |                                                         |
|-----------------|---------------------------------------------------------|
| End point title | Respiratory Rate (change from baseline) <sup>[45]</sup> |
|-----------------|---------------------------------------------------------|

End point description:

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

End point timeframe:

At all study visits (except Day 14 telephone call).

Notes:

[45] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 428             | 399             |  |  |
| Units: breaths/min                     |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 0.2 (-4 to 12)  | -0.2 (-6 to 8)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Temperature (change from baseline)

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | Temperature (change from baseline) <sup>[46]</sup> |
|-----------------|----------------------------------------------------|

End point description:

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

End point timeframe:

At all study visits (except Day 14 telephone call).

Notes:

[46] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg   | EVP-6124, 2 mg     |  |  |
|----------------------------------------|------------------|--------------------|--|--|
| Subject group type                     | Reporting group  | Reporting group    |  |  |
| Number of subjects analysed            | 428              | 399                |  |  |
| Units: celsius temperature             |                  |                    |  |  |
| arithmetic mean (full range (min-max)) | 0.02 (-1.3 to 1) | 0.02 (-1.4 to 1.6) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Weight (change from baseline)

|                 |                                               |
|-----------------|-----------------------------------------------|
| End point title | Weight (change from baseline) <sup>[47]</sup> |
|-----------------|-----------------------------------------------|

End point description:

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

End point timeframe:

At all study visits (except Day 14 telephone call).

Notes:

[47] - 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: This was a safety extension study, so there were no pre-defined statistical analysis.

| End point values                       | EVP-6124, 1 mg        | EVP-6124, 2 mg        |  |  |
|----------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                     | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed            | 428                   | 399                   |  |  |
| Units: kilogram(s)                     |                       |                       |  |  |
| arithmetic mean (full range (min-max)) | -0.45 (-19.9 to 13.5) | -0.04 (-19.1 to 11.3) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: CGI-S severity scores (change from baseline)

|                 |                                              |
|-----------------|----------------------------------------------|
| End point title | CGI-S severity scores (change from baseline) |
|-----------------|----------------------------------------------|

End point description:

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

End point timeframe:

On Days 56, 112, and 182, or ET.

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 421             | 388             |  |  |
| Units: n/a                             |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | -0.1 (-2 to 2)  | -0.1 (-2 to 3)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: CGI-C change scores (Day 182)

|                                  |                               |
|----------------------------------|-------------------------------|
| End point title                  | CGI-C change scores (Day 182) |
| End point description:           |                               |
| End point type                   | Secondary                     |
| End point timeframe:             |                               |
| On Days 56, 112, and 182, or ET. |                               |

| End point values                       | EVP-6124, 1 mg  | EVP-6124, 2 mg  |  |  |
|----------------------------------------|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 421             | 388             |  |  |
| Units: n/a                             |                 |                 |  |  |
| arithmetic mean (full range (min-max)) | 3.1 (1 to 6)    | 3.1 (1 to 7)    |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Concentration of EVP-6124 (Day 182)

|                                      |                                     |
|--------------------------------------|-------------------------------------|
| End point title                      | Concentration of EVP-6124 (Day 182) |
| End point description:               |                                     |
| End point type                       | Other pre-specified                 |
| End point timeframe:                 |                                     |
| On Days 28, 56, 112, and 182, or ET. |                                     |

| End point values                       | EVP-6124, 1 mg      | EVP-6124, 2 mg      |  |  |
|----------------------------------------|---------------------|---------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed            | 427                 | 394                 |  |  |
| Units: ng/ml                           |                     |                     |  |  |
| arithmetic mean (full range (min-max)) | 1.59224 (0 to 5.06) | 3.13547 (0 to 9.45) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Concentration of EVP-6124 N-Oxide Metabolite (Day 182)

|                 |                                                        |
|-----------------|--------------------------------------------------------|
| End point title | Concentration of EVP-6124 N-Oxide Metabolite (Day 182) |
|-----------------|--------------------------------------------------------|

End point description:

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

On Days 28, 56, 112, and 182, or ET.

| End point values                       | EVP-6124, 1 mg       | EVP-6124, 2 mg      |  |  |
|----------------------------------------|----------------------|---------------------|--|--|
| Subject group type                     | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed            | 427                  | 394                 |  |  |
| Units: ng/ml                           |                      |                     |  |  |
| arithmetic mean (full range (min-max)) | 0.17276 (0 to 0.778) | 0.30632 (0 to 1.05) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Concentration of EVP-6124 Acid Metabolite (Day 182)

|                 |                                                     |
|-----------------|-----------------------------------------------------|
| End point title | Concentration of EVP-6124 Acid Metabolite (Day 182) |
|-----------------|-----------------------------------------------------|

End point description:

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

On Days 28, 56, 112, and 182, or ET.



|                                        |                      |                     |  |  |
|----------------------------------------|----------------------|---------------------|--|--|
| <b>End point values</b>                | EVP-6124, 1 mg       | EVP-6124, 2 mg      |  |  |
| Subject group type                     | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed            | 427                  | 394                 |  |  |
| Units: ng/ml                           |                      |                     |  |  |
| arithmetic mean (full range (min-max)) | 0.22055 (0 to 0.678) | 0.44114 (0 to 2.24) |  |  |

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Throughout the study

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | EVP-6124, 1 mg |
|-----------------------|----------------|

Reporting group description:

Subjects who received EVP-6124 during the previous study (EVP-6124-015 or EVP-6124-016) will remain on the same dose. Subjects who received placebo during the pivotal study (EVP-6124-015 or EVP-6124-016) will be randomized (1:1 ratio) to once daily EVP-6124 1 or 2 mg tablets for up to 26 weeks (Days 1-182).

|                       |                |
|-----------------------|----------------|
| Reporting group title | EVP-6124, 2 mg |
|-----------------------|----------------|

Reporting group description:

Subjects who received EVP-6124 during the previous study (EVP-6124-015 or EVP-6124-016) will remain on the same dose. Subjects who received placebo during the pivotal study (EVP-6124-015 or EVP-6124-016) will be randomized (1:1 ratio) to once daily EVP-6124 1 or 2 mg tablets for up to 26 weeks (Days 1-182).

| Serious adverse events                                              | EVP-6124, 1 mg   | EVP-6124, 2 mg   |  |
|---------------------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by serious adverse events                   |                  |                  |  |
| subjects affected / exposed                                         | 12 / 428 (2.80%) | 20 / 399 (5.01%) |  |
| number of deaths (all causes)                                       | 0                | 0                |  |
| number of deaths resulting from adverse events                      |                  |                  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |  |
| Invasive ductal breast carcinoma                                    |                  |                  |  |
| subjects affected / exposed                                         | 0 / 428 (0.00%)  | 1 / 399 (0.25%)  |  |
| occurrences causally related to treatment / all                     | 0 / 12           | 0 / 20           |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |
| Investigations                                                      |                  |                  |  |
| Blood creatine phosphokinase increased                              |                  |                  |  |
| subjects affected / exposed                                         | 1 / 428 (0.23%)  | 0 / 399 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 12           | 0 / 20           |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |
| Injury, poisoning and procedural complications                      |                  |                  |  |
| Burns third degree                                                  |                  |                  |  |

|                                                      |                 |                 |  |
|------------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all      | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Multiple injuries                                    |                 |                 |  |
| subjects affected / exposed                          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all      | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Road traffic accident                                |                 |                 |  |
| subjects affected / exposed                          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all      | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Toxicity to various agents                           |                 |                 |  |
| subjects affected / exposed                          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all      | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Upper limb fracture                                  |                 |                 |  |
| subjects affected / exposed                          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all      | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Non-cardiac chest pain                               |                 |                 |  |
| subjects affected / exposed                          | 0 / 428 (0.00%) | 2 / 399 (0.50%) |  |
| occurrences causally related to treatment / all      | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Social circumstances                                 |                 |                 |  |
| Homicide                                             |                 |                 |  |
| subjects affected / exposed                          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all      | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                           |                 |                 |  |
| Abdominal hernia                                     |                 |                 |  |
| subjects affected / exposed                          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all      | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Volvulus                                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psychiatric disorders                           |                 |                 |  |
| Psychiatric decompensation                      |                 |                 |  |
| subjects affected / exposed                     | 7 / 428 (1.64%) | 7 / 399 (1.75%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 1 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Depression                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Paranoia                                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Substance abuse                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Suicidal behaviour                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Suicidal ideation                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Appendicitis                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Bronchitis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diverticulitis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 12          | 0 / 20          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                                   | EVP-6124, 1 mg     | EVP-6124, 2 mg     |  |
|---------------------------------------------------------------------|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events               |                    |                    |  |
| subjects affected / exposed                                         | 164 / 428 (38.32%) | 149 / 399 (37.34%) |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                    |  |
| Invasive ductal breast carcinoma                                    |                    |                    |  |
| subjects affected / exposed                                         | 0 / 428 (0.00%)    | 1 / 399 (0.25%)    |  |
| occurrences (all)                                                   | 164                | 149                |  |
| Vascular disorders                                                  |                    |                    |  |
| Hypertension                                                        |                    |                    |  |
| subjects affected / exposed                                         | 2 / 428 (0.47%)    | 1 / 399 (0.25%)    |  |
| occurrences (all)                                                   | 164                | 149                |  |
| Hyperaemia                                                          |                    |                    |  |
| subjects affected / exposed                                         | 0 / 428 (0.00%)    | 1 / 399 (0.25%)    |  |
| occurrences (all)                                                   | 164                | 149                |  |
| General disorders and administration site conditions                |                    |                    |  |
| Asthenia                                                            |                    |                    |  |
| subjects affected / exposed                                         | 2 / 428 (0.47%)    | 2 / 399 (0.50%)    |  |
| occurrences (all)                                                   | 164                | 149                |  |
| Fatigue                                                             |                    |                    |  |
| subjects affected / exposed                                         | 2 / 428 (0.47%)    | 2 / 399 (0.50%)    |  |
| occurrences (all)                                                   | 164                | 149                |  |
| Chest pain                                                          |                    |                    |  |
| subjects affected / exposed                                         | 1 / 428 (0.23%)    | 1 / 399 (0.25%)    |  |
| occurrences (all)                                                   | 164                | 149                |  |

|                                                                                            |                        |                        |  |
|--------------------------------------------------------------------------------------------|------------------------|------------------------|--|
| Non-cardiac chest pain<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 428 (0.00%)<br>164 | 2 / 399 (0.50%)<br>149 |  |
| Drug withdrawal syndrome<br>subjects affected / exposed<br>occurrences (all)               | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Feeling jittery<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Hernia<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Inflammation<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Injection site swelling<br>subjects affected / exposed<br>occurrences (all)                | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Malaise<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Pain<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Immune system disorders<br>Sarcoidosis<br>subjects affected / exposed<br>occurrences (all) | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Seasonal allergy                                                                           |                        |                        |  |

|                                                                                                               |                        |                        |  |
|---------------------------------------------------------------------------------------------------------------|------------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                              | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Social circumstances<br>Homicide<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Reproductive system and breast disorders<br>Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all) | 2 / 428 (0.47%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Amenorrhoea<br>subjects affected / exposed<br>occurrences (all)                                               | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Menstrual disorder<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)  | 4 / 428 (0.93%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                                               | 1 / 428 (0.23%)<br>164 | 2 / 399 (0.50%)<br>149 |  |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)                                          | 1 / 428 (0.23%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                                        | 1 / 428 (0.23%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Allergic pharyngitis<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Asthma                                                                                                        |                        |                        |  |

|                             |                  |                 |  |
|-----------------------------|------------------|-----------------|--|
| subjects affected / exposed | 1 / 428 (0.23%)  | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164              | 149             |  |
| Dyspnoea                    |                  |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%)  | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164              | 149             |  |
| Epistaxis                   |                  |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%)  | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164              | 149             |  |
| Nasal polyps                |                  |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%)  | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164              | 149             |  |
| Nocturnal dyspnoea          |                  |                 |  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%) |  |
| occurrences (all)           | 164              | 149             |  |
| Oropharyngeal discomfort    |                  |                 |  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%) |  |
| occurrences (all)           | 164              | 149             |  |
| Productive cough            |                  |                 |  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%) |  |
| occurrences (all)           | 164              | 149             |  |
| Respiratory disorder        |                  |                 |  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%) |  |
| occurrences (all)           | 164              | 149             |  |
| Respiratory distress        |                  |                 |  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%) |  |
| occurrences (all)           | 164              | 149             |  |
| Rhinitis allergic           |                  |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%)  | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164              | 149             |  |
| Sneezing                    |                  |                 |  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%) |  |
| occurrences (all)           | 164              | 149             |  |
| Psychiatric disorders       |                  |                 |  |
| Insomnia                    |                  |                 |  |
| subjects affected / exposed | 14 / 428 (3.27%) | 8 / 399 (2.01%) |  |
| occurrences (all)           | 164              | 149             |  |



|                             |                  |                  |
|-----------------------------|------------------|------------------|
| Psychiatric decompensation  |                  |                  |
| subjects affected / exposed | 8 / 428 (1.87%)  | 14 / 399 (3.51%) |
| occurrences (all)           | 164              | 149              |
| Anxiety                     |                  |                  |
| subjects affected / exposed | 10 / 428 (2.34%) | 5 / 399 (1.25%)  |
| occurrences (all)           | 164              | 149              |
| Depression                  |                  |                  |
| subjects affected / exposed | 5 / 428 (1.17%)  | 0 / 399 (0.00%)  |
| occurrences (all)           | 164              | 149              |
| Psychotic disorder          |                  |                  |
| subjects affected / exposed | 3 / 428 (0.70%)  | 2 / 399 (0.50%)  |
| occurrences (all)           | 164              | 149              |
| Suicidal ideation           |                  |                  |
| subjects affected / exposed | 3 / 428 (0.70%)  | 2 / 399 (0.50%)  |
| occurrences (all)           | 164              | 149              |
| Irritability                |                  |                  |
| subjects affected / exposed | 2 / 428 (0.47%)  | 2 / 399 (0.50%)  |
| occurrences (all)           | 164              | 149              |
| Panic attack                |                  |                  |
| subjects affected / exposed | 3 / 428 (0.70%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Initial insomnia            |                  |                  |
| subjects affected / exposed | 2 / 428 (0.47%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Agitation                   |                  |                  |
| subjects affected / exposed | 2 / 428 (0.47%)  | 0 / 399 (0.00%)  |
| occurrences (all)           | 164              | 149              |
| Delusion                    |                  |                  |
| subjects affected / exposed | 2 / 428 (0.47%)  | 0 / 399 (0.00%)  |
| occurrences (all)           | 164              | 149              |
| Depressed mood              |                  |                  |
| subjects affected / exposed | 1 / 428 (0.23%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Restlessness                |                  |                  |
| subjects affected / exposed | 2 / 428 (0.47%)  | 0 / 399 (0.00%)  |
| occurrences (all)           | 164              | 149              |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| Abnormal dreams             |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Affect lability             |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Aggression                  |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Bruxism                     |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Hallucination               |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Hallucination, auditory     |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Hallucination, visual       |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Homicidal ideation          |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Middle insomnia             |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Paranoia                    |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Sleep disorder              |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Sleep terror                |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |

|                                        |                  |                 |  |
|----------------------------------------|------------------|-----------------|--|
| Stress                                 |                  |                 |  |
| subjects affected / exposed            | 1 / 428 (0.23%)  | 0 / 399 (0.00%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Substance abuse                        |                  |                 |  |
| subjects affected / exposed            | 1 / 428 (0.23%)  | 0 / 399 (0.00%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Suicidal behaviour                     |                  |                 |  |
| subjects affected / exposed            | 0 / 428 (0.00%)  | 1 / 399 (0.25%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Tension                                |                  |                 |  |
| subjects affected / exposed            | 1 / 428 (0.23%)  | 0 / 399 (0.00%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Investigations                         |                  |                 |  |
| Weight increased                       |                  |                 |  |
| subjects affected / exposed            | 10 / 428 (2.34%) | 7 / 399 (1.75%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Weight decreased                       |                  |                 |  |
| subjects affected / exposed            | 4 / 428 (0.93%)  | 6 / 399 (1.50%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Blood creatine phosphokinase increased |                  |                 |  |
| subjects affected / exposed            | 5 / 428 (1.17%)  | 4 / 399 (1.00%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Alanine aminotransferase increased     |                  |                 |  |
| subjects affected / exposed            | 4 / 428 (0.93%)  | 1 / 399 (0.25%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Blood glucose increased                |                  |                 |  |
| subjects affected / exposed            | 1 / 428 (0.23%)  | 4 / 399 (1.00%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Gamma-glutamyltransferase increased    |                  |                 |  |
| subjects affected / exposed            | 2 / 428 (0.47%)  | 1 / 399 (0.25%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Aspartate aminotransferase increased   |                  |                 |  |
| subjects affected / exposed            | 1 / 428 (0.23%)  | 1 / 399 (0.25%) |  |
| occurrences (all)                      | 164              | 149             |  |
| Urine leukocyte esterase positive      |                  |                 |  |

|                                                |                 |                 |  |
|------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                    | 2 / 428 (0.47%) | 0 / 399 (0.00%) |  |
| occurrences (all)                              | 164             | 149             |  |
| White blood cell count increased               |                 |                 |  |
| subjects affected / exposed                    | 1 / 428 (0.23%) | 1 / 399 (0.25%) |  |
| occurrences (all)                              | 164             | 149             |  |
| Blood bilirubin increased                      |                 |                 |  |
| subjects affected / exposed                    | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                              | 164             | 149             |  |
| Blood creatinine increased                     |                 |                 |  |
| subjects affected / exposed                    | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                              | 164             | 149             |  |
| Blood potassium decreased                      |                 |                 |  |
| subjects affected / exposed                    | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                              | 164             | 149             |  |
| Blood pressure increased                       |                 |                 |  |
| subjects affected / exposed                    | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                              | 164             | 149             |  |
| Electrocardiogram ST segment depression        |                 |                 |  |
| subjects affected / exposed                    | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                              | 164             | 149             |  |
| Electrocardiogram T wave abnormal              |                 |                 |  |
| subjects affected / exposed                    | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                              | 164             | 149             |  |
| Neutrophil count increased                     |                 |                 |  |
| subjects affected / exposed                    | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                              | 164             | 149             |  |
| White blood cells urine positive               |                 |                 |  |
| subjects affected / exposed                    | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                              | 164             | 149             |  |
| Injury, poisoning and procedural complications |                 |                 |  |
| Contusion                                      |                 |                 |  |
| subjects affected / exposed                    | 2 / 428 (0.47%) | 2 / 399 (0.50%) |  |
| occurrences (all)                              | 164             | 149             |  |
| Laceration                                     |                 |                 |  |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 428 (0.23%) | 2 / 399 (0.50%) |
| occurrences (all)           | 164             | 149             |
| Sunburn                     |                 |                 |
| subjects affected / exposed | 3 / 428 (0.70%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Fall                        |                 |                 |
| subjects affected / exposed | 2 / 428 (0.47%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Multiple injuries           |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 2 / 399 (0.50%) |
| occurrences (all)           | 164             | 149             |
| Road traffic accident       |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 2 / 399 (0.50%) |
| occurrences (all)           | 164             | 149             |
| Skin abrasion               |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 2 / 399 (0.50%) |
| occurrences (all)           | 164             | 149             |
| Wound                       |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 2 / 399 (0.50%) |
| occurrences (all)           | 164             | 149             |
| Arthropod bite              |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Burns first degree          |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Burns third degree          |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Excoriation                 |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Intentional overdose        |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Joint dislocation           |                 |                 |

|                                     |                 |                 |  |
|-------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed         | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Ligament injury                     |                 |                 |  |
| subjects affected / exposed         | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Ligament sprain                     |                 |                 |  |
| subjects affected / exposed         | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Meniscus injury                     |                 |                 |  |
| subjects affected / exposed         | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Nail injury                         |                 |                 |  |
| subjects affected / exposed         | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Spinal fracture                     |                 |                 |  |
| subjects affected / exposed         | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Toxicity to various agents          |                 |                 |  |
| subjects affected / exposed         | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Upper limb fracture                 |                 |                 |  |
| subjects affected / exposed         | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Periorbital contusion               |                 |                 |  |
| subjects affected / exposed         | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Cardiac disorders                   |                 |                 |  |
| Atrioventricular block first degree |                 |                 |  |
| subjects affected / exposed         | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Tachycardia                         |                 |                 |  |
| subjects affected / exposed         | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                   | 164             | 149             |  |
| Nervous system disorders            |                 |                 |  |
| Headache                            |                 |                 |  |

|                             |                  |                  |
|-----------------------------|------------------|------------------|
| subjects affected / exposed | 24 / 428 (5.61%) | 12 / 399 (3.01%) |
| occurrences (all)           | 164              | 149              |
| Dizziness                   |                  |                  |
| subjects affected / exposed | 6 / 428 (1.40%)  | 4 / 399 (1.00%)  |
| occurrences (all)           | 164              | 149              |
| Tremor                      |                  |                  |
| subjects affected / exposed | 2 / 428 (0.47%)  | 4 / 399 (1.00%)  |
| occurrences (all)           | 164              | 149              |
| Somnolence                  |                  |                  |
| subjects affected / exposed | 3 / 428 (0.70%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Paraesthesia                |                  |                  |
| subjects affected / exposed | 2 / 428 (0.47%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Akathisia                   |                  |                  |
| subjects affected / exposed | 1 / 428 (0.23%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Memory impairment           |                  |                  |
| subjects affected / exposed | 2 / 428 (0.47%)  | 0 / 399 (0.00%)  |
| occurrences (all)           | 164              | 149              |
| Mental impairment           |                  |                  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 2 / 399 (0.50%)  |
| occurrences (all)           | 164              | 149              |
| Bradykinesia                |                  |                  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Carpal tunnel syndrome      |                  |                  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Disturbance in attention    |                  |                  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Hypersomnia                 |                  |                  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%)  |
| occurrences (all)           | 164              | 149              |
| Hypoaesthesia               |                  |                  |

|                                      |                 |                 |  |
|--------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Intercostal neuralgia                |                 |                 |  |
| subjects affected / exposed          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Lethargy                             |                 |                 |  |
| subjects affected / exposed          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Restless legs syndrome               |                 |                 |  |
| subjects affected / exposed          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Tension headache                     |                 |                 |  |
| subjects affected / exposed          | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Blood and lymphatic system disorders |                 |                 |  |
| Neutropenia                          |                 |                 |  |
| subjects affected / exposed          | 1 / 428 (0.23%) | 1 / 399 (0.25%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Iron deficiency anaemia              |                 |                 |  |
| subjects affected / exposed          | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Leukopenia                           |                 |                 |  |
| subjects affected / exposed          | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Ear and labyrinth disorders          |                 |                 |  |
| Ear pain                             |                 |                 |  |
| subjects affected / exposed          | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Vertigo                              |                 |                 |  |
| subjects affected / exposed          | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Eye disorders                        |                 |                 |  |
| Vision blurred                       |                 |                 |  |
| subjects affected / exposed          | 1 / 428 (0.23%) | 2 / 399 (0.50%) |  |
| occurrences (all)                    | 164             | 149             |  |
| Dry eye                              |                 |                 |  |



|                             |                  |                  |  |
|-----------------------------|------------------|------------------|--|
| subjects affected / exposed | 1 / 428 (0.23%)  | 1 / 399 (0.25%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Iritis                      |                  |                  |  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Oculogyric crisis           |                  |                  |  |
| subjects affected / exposed | 1 / 428 (0.23%)  | 0 / 399 (0.00%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Scleral hyperaemia          |                  |                  |  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Vitreous floaters           |                  |                  |  |
| subjects affected / exposed | 0 / 428 (0.00%)  | 1 / 399 (0.25%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Gastrointestinal disorders  |                  |                  |  |
| Constipation                |                  |                  |  |
| subjects affected / exposed | 11 / 428 (2.57%) | 14 / 399 (3.51%) |  |
| occurrences (all)           | 164              | 149              |  |
| Diarrhoea                   |                  |                  |  |
| subjects affected / exposed | 6 / 428 (1.40%)  | 9 / 399 (2.26%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Nausea                      |                  |                  |  |
| subjects affected / exposed | 8 / 428 (1.87%)  | 3 / 399 (0.75%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Toothache                   |                  |                  |  |
| subjects affected / exposed | 4 / 428 (0.93%)  | 4 / 399 (1.00%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Abdominal pain upper        |                  |                  |  |
| subjects affected / exposed | 5 / 428 (1.17%)  | 1 / 399 (0.25%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Dyspepsia                   |                  |                  |  |
| subjects affected / exposed | 2 / 428 (0.47%)  | 4 / 399 (1.00%)  |  |
| occurrences (all)           | 164              | 149              |  |
| Abdominal pain              |                  |                  |  |
| subjects affected / exposed | 1 / 428 (0.23%)  | 3 / 399 (0.75%)  |  |
| occurrences (all)           | 164              | 149              |  |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| Vomiting                    |                 |                 |
| subjects affected / exposed | 3 / 428 (0.70%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Dry mouth                   |                 |                 |
| subjects affected / exposed | 2 / 428 (0.47%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Food poisoning              |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Abdominal hernia            |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Dental caries               |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Dysphagia                   |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Faeces hard                 |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Faeces soft                 |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Haemorrhoids                |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Large intestine polyp       |                 |                 |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)           | 164             | 149             |
| Lip blister                 |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |
| Lip pain                    |                 |                 |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)           | 164             | 149             |

|                                                                             |                        |                        |  |
|-----------------------------------------------------------------------------|------------------------|------------------------|--|
| Salivary hypersecretion<br>subjects affected / exposed<br>occurrences (all) | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Tooth impacted<br>subjects affected / exposed<br>occurrences (all)          | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Volvulus<br>subjects affected / exposed<br>occurrences (all)                | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Skin and subcutaneous tissue disorders                                      |                        |                        |  |
| Acne<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Eczema<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all)           | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Rash papular<br>subjects affected / exposed<br>occurrences (all)            | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Skin exfoliation<br>subjects affected / exposed<br>occurrences (all)        | 0 / 428 (0.00%)<br>164 | 1 / 399 (0.25%)<br>149 |  |
| Swelling face<br>subjects affected / exposed<br>occurrences (all)           | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Urticaria                                                                   |                        |                        |  |

|                                                  |                        |                        |  |
|--------------------------------------------------|------------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all) | 1 / 428 (0.23%)<br>164 | 0 / 399 (0.00%)<br>149 |  |
| Renal and urinary disorders                      |                        |                        |  |
| Hypertonic bladder                               |                        |                        |  |
| subjects affected / exposed                      | 1 / 428 (0.23%)        | 1 / 399 (0.25%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Pollakiuria                                      |                        |                        |  |
| subjects affected / exposed                      | 1 / 428 (0.23%)        | 1 / 399 (0.25%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Bladder disorder                                 |                        |                        |  |
| subjects affected / exposed                      | 1 / 428 (0.23%)        | 0 / 399 (0.00%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Cystitis haemorrhagic                            |                        |                        |  |
| subjects affected / exposed                      | 0 / 428 (0.00%)        | 1 / 399 (0.25%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Enuresis                                         |                        |                        |  |
| subjects affected / exposed                      | 0 / 428 (0.00%)        | 1 / 399 (0.25%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Haematuria                                       |                        |                        |  |
| subjects affected / exposed                      | 1 / 428 (0.23%)        | 0 / 399 (0.00%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Urine flow decreased                             |                        |                        |  |
| subjects affected / exposed                      | 0 / 428 (0.00%)        | 1 / 399 (0.25%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Endocrine disorders                              |                        |                        |  |
| Hyperprolactinaemia                              |                        |                        |  |
| subjects affected / exposed                      | 0 / 428 (0.00%)        | 2 / 399 (0.50%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Goitre                                           |                        |                        |  |
| subjects affected / exposed                      | 0 / 428 (0.00%)        | 1 / 399 (0.25%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Hypothyroidism                                   |                        |                        |  |
| subjects affected / exposed                      | 1 / 428 (0.23%)        | 0 / 399 (0.00%)        |  |
| occurrences (all)                                | 164                    | 149                    |  |
| Musculoskeletal and connective tissue disorders  |                        |                        |  |

|                                  |                 |                 |
|----------------------------------|-----------------|-----------------|
| Back pain                        |                 |                 |
| subjects affected / exposed      | 2 / 428 (0.47%) | 6 / 399 (1.50%) |
| occurrences (all)                | 164             | 149             |
| Arthralgia                       |                 |                 |
| subjects affected / exposed      | 2 / 428 (0.47%) | 2 / 399 (0.50%) |
| occurrences (all)                | 164             | 149             |
| Muscle spasms                    |                 |                 |
| subjects affected / exposed      | 2 / 428 (0.47%) | 1 / 399 (0.25%) |
| occurrences (all)                | 164             | 149             |
| Pain in extremity                |                 |                 |
| subjects affected / exposed      | 1 / 428 (0.23%) | 2 / 399 (0.50%) |
| occurrences (all)                | 164             | 149             |
| Arthritis                        |                 |                 |
| subjects affected / exposed      | 2 / 428 (0.47%) | 0 / 399 (0.00%) |
| occurrences (all)                | 164             | 149             |
| Myalgia                          |                 |                 |
| subjects affected / exposed      | 0 / 428 (0.00%) | 2 / 399 (0.50%) |
| occurrences (all)                | 164             | 149             |
| Temporomandibular joint syndrome |                 |                 |
| subjects affected / exposed      | 1 / 428 (0.23%) | 1 / 399 (0.25%) |
| occurrences (all)                | 164             | 149             |
| Coccydynia                       |                 |                 |
| subjects affected / exposed      | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)                | 164             | 149             |
| Muscle rigidity                  |                 |                 |
| subjects affected / exposed      | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)                | 164             | 149             |
| Musculoskeletal chest pain       |                 |                 |
| subjects affected / exposed      | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)                | 164             | 149             |
| Musculoskeletal pain             |                 |                 |
| subjects affected / exposed      | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)                | 164             | 149             |
| Periarthritis                    |                 |                 |
| subjects affected / exposed      | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)                | 164             | 149             |

|                                                                                                    |                         |                         |  |
|----------------------------------------------------------------------------------------------------|-------------------------|-------------------------|--|
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 13 / 428 (3.04%)<br>164 | 20 / 399 (5.01%)<br>149 |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                                      | 3 / 428 (0.70%)<br>164  | 7 / 399 (1.75%)<br>149  |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)              | 8 / 428 (1.87%)<br>164  | 2 / 399 (0.50%)<br>149  |  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                        | 7 / 428 (1.64%)<br>164  | 3 / 399 (0.75%)<br>149  |  |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                                     | 4 / 428 (0.93%)<br>164  | 2 / 399 (0.50%)<br>149  |  |
| Ear infection<br>subjects affected / exposed<br>occurrences (all)                                  | 2 / 428 (0.47%)<br>164  | 3 / 399 (0.75%)<br>149  |  |
| Pharyngitis<br>subjects affected / exposed<br>occurrences (all)                                    | 2 / 428 (0.47%)<br>164  | 2 / 399 (0.50%)<br>149  |  |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 428 (0.23%)<br>164  | 2 / 399 (0.50%)<br>149  |  |
| Abscess limb<br>subjects affected / exposed<br>occurrences (all)                                   | 2 / 428 (0.47%)<br>164  | 0 / 399 (0.00%)<br>149  |  |
| Cellulitis<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 428 (0.00%)<br>164  | 2 / 399 (0.50%)<br>149  |  |
| Gastroenteritis viral<br>subjects affected / exposed<br>occurrences (all)                          | 2 / 428 (0.47%)<br>164  | 0 / 399 (0.00%)<br>149  |  |
| Pneumonia                                                                                          |                         |                         |  |

|                                         |                 |                 |
|-----------------------------------------|-----------------|-----------------|
| subjects affected / exposed             | 2 / 428 (0.47%) | 0 / 399 (0.00%) |
| occurrences (all)                       | 164             | 149             |
| Respiratory tract infection             |                 |                 |
| subjects affected / exposed             | 1 / 428 (0.23%) | 1 / 399 (0.25%) |
| occurrences (all)                       | 164             | 149             |
| Sinusitis                               |                 |                 |
| subjects affected / exposed             | 1 / 428 (0.23%) | 1 / 399 (0.25%) |
| occurrences (all)                       | 164             | 149             |
| Viral upper respiratory tract infection |                 |                 |
| subjects affected / exposed             | 0 / 428 (0.00%) | 2 / 399 (0.50%) |
| occurrences (all)                       | 164             | 149             |
| Appendicitis                            |                 |                 |
| subjects affected / exposed             | 0 / 428 (0.00%) | 2 / 399 (0.50%) |
| occurrences (all)                       | 164             | 149             |
| Conjunctivitis                          |                 |                 |
| subjects affected / exposed             | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)                       | 164             | 149             |
| Diverticulitis                          |                 |                 |
| subjects affected / exposed             | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)                       | 164             | 149             |
| Folliculitis                            |                 |                 |
| subjects affected / exposed             | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)                       | 164             | 149             |
| Furuncle                                |                 |                 |
| subjects affected / exposed             | 1 / 428 (0.23%) | 0 / 399 (0.00%) |
| occurrences (all)                       | 164             | 149             |
| Gingivitis                              |                 |                 |
| subjects affected / exposed             | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)                       | 164             | 149             |
| Helicobacter gastritis                  |                 |                 |
| subjects affected / exposed             | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)                       | 164             | 149             |
| Hordeolum                               |                 |                 |
| subjects affected / exposed             | 0 / 428 (0.00%) | 1 / 399 (0.25%) |
| occurrences (all)                       | 164             | 149             |
| Infected bites                          |                 |                 |

|                                    |                 |                 |  |
|------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed        | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Laryngitis                         |                 |                 |  |
| subjects affected / exposed        | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Otitis externa                     |                 |                 |  |
| subjects affected / exposed        | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Otitis media                       |                 |                 |  |
| subjects affected / exposed        | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Pharyngitis streptococcal          |                 |                 |  |
| subjects affected / exposed        | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Respiratory tract infection viral  |                 |                 |  |
| subjects affected / exposed        | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Skin candida                       |                 |                 |  |
| subjects affected / exposed        | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Subcutaneous abscess               |                 |                 |  |
| subjects affected / exposed        | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Tonsillitis                        |                 |                 |  |
| subjects affected / exposed        | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Tooth abscess                      |                 |                 |  |
| subjects affected / exposed        | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Tooth infection                    |                 |                 |  |
| subjects affected / exposed        | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Varicella                          |                 |                 |  |
| subjects affected / exposed        | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)                  | 164             | 149             |  |
| Metabolism and nutrition disorders |                 |                 |  |



|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| Hyperglycaemia              |                 |                 |  |
| subjects affected / exposed | 2 / 428 (0.47%) | 1 / 399 (0.25%) |  |
| occurrences (all)           | 164             | 149             |  |
| Increased appetite          |                 |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%) | 2 / 399 (0.50%) |  |
| occurrences (all)           | 164             | 149             |  |
| Vitamin D deficiency        |                 |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%) | 1 / 399 (0.25%) |  |
| occurrences (all)           | 164             | 149             |  |
| Decreased appetite          |                 |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164             | 149             |  |
| Food craving                |                 |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164             | 149             |  |
| Gout                        |                 |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164             | 149             |  |
| Hypercholesterolaemia       |                 |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164             | 149             |  |
| Hyperlipidaemia             |                 |                 |  |
| subjects affected / exposed | 1 / 428 (0.23%) | 0 / 399 (0.00%) |  |
| occurrences (all)           | 164             | 149             |  |
| Type 2 diabetes mellitus    |                 |                 |  |
| subjects affected / exposed | 0 / 428 (0.00%) | 1 / 399 (0.25%) |  |
| occurrences (all)           | 164             | 149             |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date           | Amendment                               |
|----------------|-----------------------------------------|
| 08 March 2013  | Protocol Amendment 1 (08 March 2013)    |
| 02 August 2013 | Protocol Amendment 2 (02 August 2013)   |
| 26 August 2014 | Protocol Amendment 2.1 (26 August 2014) |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported