

**Clinical trial results:****An open-label treatment study to evaluate the safety, tolerability and efficacy of AFQ056 in Parkinson's patients with L-dopa induced dyskinesias****Summary**

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2011-004378-27    |
| Trial protocol           | ES HU DE IT SK AT |
| Global end of trial date | 04 November 2013  |

**Results information**

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 13 July 2016   |
| First version publication date | 01 August 2015 |

**Trial information****Trial identification**

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CAFQ056A2299 |
|-----------------------|--------------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01491932 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novartis Pharma AG  |
| Sponsor organisation address | CH-4002 , Basel, Switzerland,                                     |
| Public contact               | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111<br>, |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111<br>, |

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                       | 04 November 2013 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 04 November 2013 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of AFQ056 in patients with PD-LID as assessed by  
•Incidence and severity of adverse events and serious adverse events •Changes in vital signs, laboratory assessments, and ECGs •Changes in underlying symptoms of PD as measured by the UPDRS (Unified Parkinson's Disease Rating Scale) part III (Motor Examination) and AEs potentially related to an exacerbation of the movement disorder of PD

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 09 March 2012 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Canada: 5        |
| Country: Number of subjects enrolled | Slovakia: 4      |
| Country: Number of subjects enrolled | Spain: 32        |
| Country: Number of subjects enrolled | Austria: 4       |
| Country: Number of subjects enrolled | France: 11       |
| Country: Number of subjects enrolled | Germany: 33      |
| Country: Number of subjects enrolled | Hungary: 5       |
| Country: Number of subjects enrolled | Italy: 28        |
| Country: Number of subjects enrolled | United States: 5 |
| Country: Number of subjects enrolled | Switzerland: 2   |
| Worldwide total number of subjects   | 129              |
| EEA total number of subjects         | 117              |

Notes:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| 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)                      | 53 |
| From 65 to 84 years                       | 76 |
| 85 years and over                         | 0  |

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## Subject disposition

### Recruitment

Recruitment details:

Patients who completed a previous core study and met the inclusion/exclusion criteria entered the open-label treatment phase.

### Pre-assignment

Screening details:

Patients who entered into this open-label treatment study within one week of completion of the last entered the study directly and the screening and baseline visit was performed on the same day. If more than one week after completion of the last visit of the core study; patients underwent a separate screening and baseline visit .

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Open-label Treatment Period (overall period) |
| Is this the baseline period? | Yes  |
| Allocation method            | Not applicable                               |
| Blinding used                | Not blinded                                  |

### Arms

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

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | AFQ056 25 mg b.i.d. |
|------------------|---------------------|

Arm description:

AFQ056 25 mg for oral administration

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | AFQ056        |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

The investigational drug, AFQ056, was provided as hard gelatin capsules. All patients took one capsule in the morning and in the evening.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | AFQ056 50 mg b.i.d. |
|------------------|---------------------|

Arm description:

AFQ056 50 mg for oral administration

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | AFQ056        |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

The investigational drug, AFQ056, was provided as hard gelatin capsules. All patients took one capsule in the morning and in the evening.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | AFQ056 75 mg b.i.d. |
|------------------|---------------------|

Arm description:

AFQ056 75 mg for oral administration

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |               |
|--|---------------|
| Investigational medicinal product name | AFQ056        |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

The investigational drug, AFQ056, was provided as hard gelatin capsules. All patients took one capsule in the morning and in the evening.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | AFQ056 100 mg b.i.d. |
|------------------|----------------------|

Arm description:

AFQ056 100 mg for oral administration

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | AFQ056        |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

The investigational drug, AFQ056, was provided as hard gelatin capsules. All patients took one capsule in the morning and in the evening.

| <b>Number of subjects in period 1</b> | AFQ056 25 mg b.i.d. | AFQ056 50 mg b.i.d. | AFQ056 75 mg b.i.d. |
|---------------------------------------|---------------------|---------------------|---------------------|
| Started                               | 20                  | 20                  | 20                  |
| Completed                             | 0                   | 0                   | 0                   |
| Not completed                         | 20                  | 20                  | 20                  |
| Physician decision                    | 1                   | 1                   | -                   |
| Study Terminated By Sponsor           | 10                  | 10                  | 17                  |
| Adverse event, non-fatal              | 5                   | 7                   | 2                   |
| Subject/Guardian Decision             | 2                   | 1                   | -                   |
| 'New Therapy For Study Indication '   | 1                   | -                   | -                   |
| Lost to follow-up                     | 1                   | -                   | 1                   |
| Protocol deviation                    | -                   | 1                   | -                   |
| Lack of efficacy                      | -                   | -                   | -                   |

| <b>Number of subjects in period 1</b> | AFQ056 100 mg b.i.d. |
|---------------------------------------|----------------------|
| Started                               | 69                   |
| Completed                             | 0                    |
| Not completed                         | 69                   |
| Physician decision                    | 1                    |
| Study Terminated By Sponsor           | 47                   |
| Adverse event, non-fatal              | 13                   |
| Subject/Guardian Decision             | 1                    |

|                                     |   |
|-------------------------------------|---|
| 'New Therapy For Study Indication ' | - |
| Lost to follow-up                   | - |
| Protocol deviation                  | - |
| Lack of efficacy                    | 7 |

## Baseline characteristics

### Reporting groups

|   |                      |
|---|----------------------|
| Reporting group title   | AFQ056 25 mg b.i.d.  |
| Reporting group description:<br>AFQ056 25 mg for oral administration  |                      |
| Reporting group title   | AFQ056 50 mg b.i.d.  |
| Reporting group description:<br>AFQ056 50 mg for oral administration  |                      |
| Reporting group title   | AFQ056 75 mg b.i.d.  |
| Reporting group description:<br>AFQ056 75 mg for oral administration  |                      |
| Reporting group title   | AFQ056 100 mg b.i.d. |
| Reporting group description:<br>AFQ056 100 mg for oral administration |                      |

| Reporting group values                | AFQ056 25 mg b.i.d. | AFQ056 50 mg b.i.d. | AFQ056 75 mg b.i.d. |
|---------------------------------------|---------------------|---------------------|---------------------|
| Number of subjects                    | 20                  | 20                  | 20                  |
| Age categorical<br>Units: Subjects    |                     |                     |                     |
| Adults (18-64 years)                  |                     |                     |                     |
| From 65-84 years                      |                     |                     |                     |
| Age continuous<br>Units: years        |                     |                     |                     |
| arithmetic mean                       | 65.9                | 67.5                | 62.9                |
| standard deviation                    | ± 8.69              | ± 7.93              | ± 8.64              |
| Gender categorical<br>Units: Subjects |                     |                     |                     |
| Female                                | 7                   | 13                  | 6                   |
| Male                                  | 13                  | 7                   | 14                  |

| Reporting group values                | AFQ056 100 mg<br>b.i.d. | Total |  |
|---------------------------------------|-------------------------|-------|--|
| Number of subjects                    | 69                      | 129   |  |
| Age categorical<br>Units: Subjects    |                         |       |  |
| Adults (18-64 years)                  |                         | 0     |  |
| From 65-84 years                      |                         | 0     |  |
| Age continuous<br>Units: years        |                         |       |  |
| arithmetic mean                       | 65.9                    | -     |  |
| standard deviation                    | ± 8.79                  |       |  |
| Gender categorical<br>Units: Subjects |                         |       |  |
| Female                                | 29                      | 55    |  |
| Male                                  | 40                      | 74    |  |

## End points

### End points reporting groups

|                                   |  |
|-----------------------------------|--|
| Reporting group title             | AFQ056 25 mg b.i.d.  |
| Reporting group description:      | AFQ056 25 mg for oral administration   |
| Reporting group title             | AFQ056 50 mg b.i.d.  |
| Reporting group description:      | AFQ056 50 mg for oral administration   |
| Reporting group title             | AFQ056 75 mg b.i.d.  |
| Reporting group description:      | AFQ056 75 mg for oral administration   |
| Reporting group title             | AFQ056 100 mg b.i.d.   |
| Reporting group description:      | AFQ056 100 mg for oral administration  |
| Subject analysis set title        | Full Analysis Set (FAS)  |
| Subject analysis set type         | Full analysis  |
| Subject analysis set description: | The FAS included all patients who received at least one dose of study medication during this open-label study.   |
| Subject analysis set title        | Safety Set (SS)  |
| Subject analysis set type         | Safety analysis  |
| Subject analysis set description: | The SS consisted of all patients who received at least one dose of open-label study drug during this open-label study and who had at least one post- baseline safety assessment. |

### Primary: Percentage of patients with at least one treatment emergent AEs

|                        |   |
|------------------------|---|
| End point title        | Percentage of patients with at least one treatment emergent AEs <sup>[1]</sup>  |
| End point description: | Treatment-emergent adverse event (TEAE) was defined as any AE newly occurred or worsened in severity after starting study drug during the open-label treatment phase. |
| End point type         | Primary   |
| End point timeframe:   | From Baseline for duration of study until early termination (04Nov2013)   |

Notes:

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

Justification: No additional statistical analyses have been performed for this primary end point.

| End point values                  | AFQ056 25 mg b.i.d. | AFQ056 50 mg b.i.d. | AFQ056 75 mg b.i.d. | AFQ056 100 mg b.i.d. |
|-----------------------------------|---------------------|---------------------|---------------------|----------------------|
| Subject group type                | Reporting group     | Reporting group     | Reporting group     | Reporting group      |
| Number of subjects analysed       | 20                  | 20                  | 20                  | 69                   |
| Units: Percentage of participants |                     |                     |                     |                      |
| number (not applicable)           | 90                  | 95                  | 100                 | 72.5                 |

## Statistical analyses

No statistical analyses for this end point

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### Primary: Summary of severity of adverse events including serious adverse events

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|                 |   |
|-----------------|---|
| End point title | Summary of severity of adverse events including serious adverse events <sup>[2]</sup> |
|-----------------|---|

End point description:

The occurrence and severity of adverse events would be sought by non-directive questioning of the patient at each visit. Adverse events may also be detected when they are volunteered by the patient during or between visits or through physical examination, laboratory test, or other assessment.

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

End point timeframe:

From Baseline for duration of study until early termination (04Nov2013)

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: No additional statistical analyses have been performed for this primary end point.

| End point values            | AFQ056 25 mg<br>b.i.d. | AFQ056 50 mg<br>b.i.d. | AFQ056 75 mg<br>b.i.d. | AFQ056 100<br>mg b.i.d. |
|-----------------------------|------------------------|------------------------|------------------------|-------------------------|
| Subject group type          | Reporting group        | Reporting group        | Reporting group        | Reporting group         |
| Number of subjects analysed | 18 <sup>[3]</sup>      | 19 <sup>[4]</sup>      | 20 <sup>[5]</sup>      | 50 <sup>[6]</sup>       |
| Units: percentage           |                        |                        |                        |                         |
| number (not applicable)     |                        |                        |                        |                         |
| Mild                        | 35                     | 15                     | 45                     | 21.7                    |
| Moderate                    | 30                     | 65                     | 45                     | 30.4                    |
| Severe                      | 25                     | 15                     | 10                     | 20.3                    |

Notes:

[3] - Patients with any AE

[4] - Patients with any AE

[5] - Patients with any AE

[6] - Patients with any AE

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### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All other adverse events are monitored from First Patient First Treatment until Last Patient Last Visit.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 16.1   |

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | AFQ056 25 MG |
|-----------------------|--------------|

Reporting group description:

AFQ056 25 MG

|                       |              |
|-----------------------|--------------|
| Reporting group title | AFQ056 50 MG |
|-----------------------|--------------|

Reporting group description:

AFQ056 50 MG

|                       |              |
|-----------------------|--------------|
| Reporting group title | AFQ056 75 MG |
|-----------------------|--------------|

Reporting group description:

AFQ056 75 MG

|                       |               |
|-----------------------|---------------|
| Reporting group title | AFQ056 100 MG |
|-----------------------|---------------|

Reporting group description:

AFQ056 100 MG

| <b>Serious adverse events</b>                     | AFQ056 25 MG    | AFQ056 50 MG    | AFQ056 75 MG    |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events |                 |                 |                 |
| subjects affected / exposed                       | 2 / 20 (10.00%) | 6 / 20 (30.00%) | 2 / 20 (10.00%) |
| number of deaths (all causes)                     | 0               | 0               | 0               |
| number of deaths resulting from adverse events    | 0               | 0               | 0               |
| Investigations                                    |                 |                 |                 |
| FIBRIN D DIMER INCREASED                          |                 |                 |                 |
| subjects affected / exposed                       | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 0           |
| Injury, poisoning and procedural complications    |                 |                 |                 |
| CERVICAL VERTEBRAL FRACTURE                       |                 |                 |                 |
| subjects affected / exposed                       | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 0           |
| FEMORAL NECK FRACTURE                             |                 |                 |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>FEMUR FRACTURE</b>                           |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>FRACTURED SACRUM</b>                         |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>HAND FRACTURE</b>                            |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>HUMERUS FRACTURE</b>                         |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>PELVIC FRACTURE</b>                          |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>RIB FRACTURE</b>                             |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>SKULL FRACTURED BASE</b>                     |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>TENDON RUPTURE</b>                           |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>ULNA FRACTURE</b>                            |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Vascular disorders</b>                       |                |                |                |
| <b>HYPOTENSION</b>                              |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Cardiac disorders</b>                        |                |                |                |
| <b>MYOCARDIAL INFARCTION</b>                    |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Nervous system disorders</b>                 |                |                |                |
| <b>AKINESIA</b>                                 |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>DYSKINESIA</b>                               |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>EPILEPSY</b>                                 |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>FREEZING PHENOMENON</b>                      |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| <b>ISCHAEMIC STROKE</b>                         |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>METABOLIC ENCEPHALOPATHY</b>                 |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>NYSTAGMUS</b>                                |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>ON AND OFF PHENOMENON</b>                    |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>PARKINSON'S DISEASE</b>                      |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Blood and lymphatic system disorders</b>     |                |                |                |
| <b>IRON DEFICIENCY ANAEMIA</b>                  |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Ear and labyrinth disorders</b>              |                |                |                |
| <b>SUDDEN HEARING LOSS</b>                      |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Gastrointestinal disorders</b>               |                |                |                |
| <b>ABDOMINAL PAIN UPPER</b>                     |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                            | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>INGUINAL HERNIA, OBSTRUCTIVE</b>                    |                |                |                |
| subjects affected / exposed                            | 1 / 20 (5.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Respiratory, thoracic and mediastinal disorders</b> |                |                |                |
| <b>DIAPHRAGMATIC RUPTURE</b>                           |                |                |                |
| subjects affected / exposed                            | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>DYSPNOEA</b>  |                |                |                |
| subjects affected / exposed                            | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Psychiatric disorders</b>                           |                |                |                |
| <b>APATHY</b>  |                |                |                |
| subjects affected / exposed                            | 1 / 20 (5.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>HALLUCINATION</b>                                   |                |                |                |
| subjects affected / exposed                            | 1 / 20 (5.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all        | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>MENTAL STATUS CHANGES</b>                           |                |                |                |
| subjects affected / exposed                            | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Musculoskeletal and connective tissue disorders</b> |                |                |                |
| <b>CERVICAL SPINAL STENOSIS</b>                        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>INTERVERTEBRAL DISC DEGENERATION</b>         |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>SPINAL COLUMN STENOSIS</b>                   |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>SYNOVIAL CYST</b>                            |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Metabolism and nutrition disorders</b>       |                |                |                |
| <b>HYPOVOLAEMIA</b>                             |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|  |                  |  |  |
|--|------------------|--|--|
| <b>Serious adverse events</b>                            | AFQ056 100 MG    |  |  |
| <b>Total subjects affected by serious adverse events</b> |                  |  |  |
| subjects affected / exposed                              | 16 / 69 (23.19%) |  |  |
| number of deaths (all causes)                            | 0                |  |  |
| number of deaths resulting from adverse events           | 0                |  |  |
| <b>Investigations</b>                                    |                  |  |  |
| <b>FIBRIN D DIMER INCREASED</b>                          |                  |  |  |
| subjects affected / exposed                              | 0 / 69 (0.00%)   |  |  |
| occurrences causally related to treatment / all          | 0 / 0            |  |  |
| deaths causally related to treatment / all               | 0 / 0            |  |  |
| <b>Injury, poisoning and procedural complications</b>    |                  |  |  |
| <b>CERVICAL VERTEBRAL FRACTURE</b>                       |                  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>FEMORAL NECK FRACTURE</b>                    |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>FEMUR FRACTURE</b>                           |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>FRACTURED SACRUM</b>                         |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>HAND FRACTURE</b>                            |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>HUMERUS FRACTURE</b>                         |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>PELVIC FRACTURE</b>                          |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>RIB FRACTURE</b>                             |                |  |  |
| subjects affected / exposed                     | 2 / 69 (2.90%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>SKULL FRACTURED BASE</b>                     |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>TENDON RUPTURE</b>                           |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>ULNA FRACTURE</b>                            |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Vascular disorders</b>                       |                |  |  |
| <b>HYPOTENSION</b>                              |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Cardiac disorders</b>                        |                |  |  |
| <b>MYOCARDIAL INFARCTION</b>                    |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Nervous system disorders</b>                 |                |  |  |
| <b>AKINESIA</b>                                 |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>DYSKINESIA</b>                               |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>EPILEPSY</b>                                 |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|   |                |  |  |
|---|----------------|--|--|
| FREEZING PHENOMENON                             |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| ISCHAEMIC STROKE                                |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| METABOLIC ENCEPHALOPATHY                        |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| NYSTAGMUS                                       |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| ON AND OFF PHENOMENON                           |                |  |  |
| subjects affected / exposed                     | 2 / 69 (2.90%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| PARKINSON'S DISEASE                             |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood and lymphatic system disorders            |                |  |  |
| IRON DEFICIENCY ANAEMIA                         |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Ear and labyrinth disorders                     |                |  |  |
| SUDDEN HEARING LOSS                             |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Gastrointestinal disorders                      |                |  |  |
| ABDOMINAL PAIN UPPER                            |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| INGUINAL HERNIA, OBSTRUCTIVE                    |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| DIAPHRAGMATIC RUPTURE                           |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| DYSпноEA  |                |  |  |
| subjects affected / exposed                     | 2 / 69 (2.90%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Psychiatric disorders                           |                |  |  |
| APATHY  |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| HALLUCINATION                                   |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| MENTAL STATUS CHANGES                           |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| CERVICAL SPINAL STENOSIS                        |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>INTERVERTEBRAL DISC DEGENERATION</b>         |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>SPINAL COLUMN STENOSIS</b>                   |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>SYNOVIAL CYST</b>                            |                |  |  |
| subjects affected / exposed                     | 0 / 69 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Metabolism and nutrition disorders</b>       |                |  |  |
| <b>HYPOVOLAEMIA</b>                             |                |  |  |
| subjects affected / exposed                     | 1 / 69 (1.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                            | AFQ056 25 MG     | AFQ056 50 MG     | AFQ056 75 MG      |
|--|------------------|------------------|-------------------|
| <b>Total subjects affected by non-serious adverse events</b> |                  |                  |                   |
| subjects affected / exposed                                  | 18 / 20 (90.00%) | 18 / 20 (90.00%) | 20 / 20 (100.00%) |
| <b>Vascular disorders</b>                                    |                  |                  |                   |
| <b>CIRCULATORY COLLAPSE</b>                                  |                  |                  |                   |
| subjects affected / exposed                                  | 0 / 20 (0.00%)   | 1 / 20 (5.00%)   | 0 / 20 (0.00%)    |
| occurrences (all)  | 0                | 1                | 0                 |
| <b>DEEP VEIN THROMBOSIS</b>                                  |                  |                  |                   |
| subjects affected / exposed                                  | 0 / 20 (0.00%)   | 1 / 20 (5.00%)   | 0 / 20 (0.00%)    |
| occurrences (all)  | 0                | 1                | 0                 |
| <b>HYPERTENSION</b>  |                  |                  |                   |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                                 | 0 / 20 (0.00%)  | 2 / 20 (10.00%) | 2 / 20 (10.00%) |
| occurrences (all)   | 0               | 3               | 2               |
| <b>HYPOTENSION</b>  |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 20 (0.00%)  | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)   | 0               | 0               | 2               |
| <b>ORTHOSTATIC HYPOTENSION</b>                              |                 |                 |                 |
| subjects affected / exposed                                 | 2 / 20 (10.00%) | 0 / 20 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 3               | 0               | 0               |
| <b>RAYNAUD'S PHENOMENON</b>                                 |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 0               | 1               | 0               |
| <b>THROMBOPHLEBITIS SUPERFICIAL</b>                         |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 0               | 1               | 0               |
| <b>General disorders and administration site conditions</b> |                 |                 |                 |
| <b>ASTHENIA</b>   |                 |                 |                 |
| subjects affected / exposed                                 | 1 / 20 (5.00%)  | 1 / 20 (5.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)   | 1               | 1               | 1               |
| <b>DEVICE DISLOCATION</b>                                   |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 0               | 1               | 0               |
| <b>FATIGUE</b>  |                 |                 |                 |
| subjects affected / exposed                                 | 2 / 20 (10.00%) | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)   | 2               | 0               | 1               |
| <b>GAIT DISTURBANCE</b>                                     |                 |                 |                 |
| subjects affected / exposed                                 | 1 / 20 (5.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 1               | 1               | 0               |
| <b>NON-CARDIAC CHEST PAIN</b>                               |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 0               | 1               | 0               |
| <b>OEDEMA PERIPHERAL</b>                                    |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 20 (0.00%)  | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)   | 0               | 0               | 1               |
| <b>PYREXIA</b>  |                 |                 |                 |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders  |                      |                      |                      |
| DYSPHONIA  |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| DYSPNOEA   |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 2 / 20 (10.00%)<br>2 | 1 / 20 (5.00%)<br>1  |
| PULMONARY ARTERIAL<br>HYPERTENSION               |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| PULMONARY EMBOLISM                               |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| RESPIRATORY DISTRESS                             |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| Psychiatric disorders                            |                      |                      |                      |
| ABNORMAL DREAMS                                  |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 2 / 20 (10.00%)<br>2 | 2 / 20 (10.00%)<br>2 | 1 / 20 (5.00%)<br>1  |
| ANXIETY  |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  |
| APATHY   |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1  | 1 / 20 (5.00%)<br>1  | 1 / 20 (5.00%)<br>1  |
| COMPULSIVE SHOPPING                              |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  |
| CONFUSIONAL STATE                                |                      |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 3 / 20 (15.00%)<br>3 | 3 / 20 (15.00%)<br>4 | 3 / 20 (15.00%)<br>3 |
| DELIRIUM   |                      |                      |                      |

|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| DEPRESSED MOOD<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| DEPRESSION<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 2 / 20 (10.00%)<br>2 |
| HALLUCINATION, AUDITORY<br>subjects affected / exposed<br>occurrences (all)               | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| HALLUCINATION, VISUAL<br>subjects affected / exposed<br>occurrences (all)                 | 3 / 20 (15.00%)<br>6 | 5 / 20 (25.00%)<br>6 | 4 / 20 (20.00%)<br>4 |
| ILLUSION<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 20 (5.00%)<br>1  | 4 / 20 (20.00%)<br>5 | 3 / 20 (15.00%)<br>3 |
| INSOMNIA<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 20 (5.00%)<br>1  | 1 / 20 (5.00%)<br>1  | 2 / 20 (10.00%)<br>2 |
| LIBIDO INCREASED<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  |
| NIGHTMARE<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| RAPID EYE MOVEMENTS SLEEP<br>ABNORMAL<br>subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| SLEEP DISORDER<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 1 / 20 (5.00%)<br>1  |
| Investigations<br>AMYLASE INCREASED   |                      |                      |                      |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                           | 0 / 20 (0.00%) | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                     | 0              | 1               | 0               |
| <b>BLOOD PRESSURE INCREASED</b>                       |                |                 |                 |
| subjects affected / exposed                           | 1 / 20 (5.00%) | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                                     | 1              | 0               | 1               |
| <b>BLOOD TRIGLYCERIDES INCREASED</b>                  |                |                 |                 |
| subjects affected / exposed                           | 1 / 20 (5.00%) | 0 / 20 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                     | 1              | 0               | 0               |
| <b>CARDIAC MURMUR</b>                                 |                |                 |                 |
| subjects affected / exposed                           | 0 / 20 (0.00%) | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                                     | 0              | 0               | 1               |
| <b>HAEMATOCRIT DECREASED</b>                          |                |                 |                 |
| subjects affected / exposed                           | 0 / 20 (0.00%) | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                     | 0              | 1               | 0               |
| <b>HAEMOGLOBIN DECREASED</b>                          |                |                 |                 |
| subjects affected / exposed                           | 0 / 20 (0.00%) | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                     | 0              | 1               | 0               |
| <b>RED BLOOD CELL COUNT DECREASED</b>                 |                |                 |                 |
| subjects affected / exposed                           | 0 / 20 (0.00%) | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                     | 0              | 1               | 0               |
| <b>WEIGHT DECREASED</b>                               |                |                 |                 |
| subjects affected / exposed                           | 0 / 20 (0.00%) | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                                     | 0              | 0               | 1               |
| <b>Injury, poisoning and procedural complications</b> |                |                 |                 |
| <b>BONE CONTUSION</b>                                 |                |                 |                 |
| subjects affected / exposed                           | 0 / 20 (0.00%) | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                                     | 0              | 1               | 0               |
| <b>EXCORIATION</b>                                    |                |                 |                 |
| subjects affected / exposed                           | 0 / 20 (0.00%) | 2 / 20 (10.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                                     | 0              | 2               | 0               |
| <b>FALL</b>   |                |                 |                 |
| subjects affected / exposed                           | 1 / 20 (5.00%) | 4 / 20 (20.00%) | 2 / 20 (10.00%) |
| occurrences (all)                                     | 1              | 8               | 2               |
| <b>HAND FRACTURE</b>                                  |                |                 |                 |

|  |                      |                     |                      |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  |
| <b>HEAD INJURY</b>                               |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  |
| <b>PERIORBITAL HAEMATOMA</b>                     |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  |
| <b>THERMAL BURN</b>                              |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  |
| <b>WOUND</b>                                     |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  |
| <b>Cardiac disorders</b>                         |                      |                     |                      |
| <b>CONDUCTION DISORDER</b>                       |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  |
| <b>DIASTOLIC DYSFUNCTION</b>                     |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  |
| <b>PALPITATIONS</b>                              |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  |
| <b>Nervous system disorders</b>                  |                      |                     |                      |
| <b>AKINESIA</b>                                  |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 5 / 20 (25.00%)<br>6 | 1 / 20 (5.00%)<br>1 | 1 / 20 (5.00%)<br>2  |
| <b>BRADYKINESIA</b>                              |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 2 / 20 (10.00%)<br>3 |
| <b>COGNITIVE DISORDER</b>                        |                      |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  |
| <b>DISTURBANCE IN ATTENTION</b>                  |                      |                     |                      |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed      | 0 / 20 (0.00%)  | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                | 0               | 0               | 1               |
| <b>DIZZINESS</b>                 |                 |                 |                 |
| subjects affected / exposed      | 2 / 20 (10.00%) | 2 / 20 (10.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                | 3               | 2               | 1               |
| <b>DYSKINESIA</b>                |                 |                 |                 |
| subjects affected / exposed      | 0 / 20 (0.00%)  | 3 / 20 (15.00%) | 2 / 20 (10.00%) |
| occurrences (all)                | 0               | 4               | 3               |
| <b>FREEZING PHENOMENON</b>       |                 |                 |                 |
| subjects affected / exposed      | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                | 0               | 1               | 1               |
| <b>HEADACHE</b>                  |                 |                 |                 |
| subjects affected / exposed      | 0 / 20 (0.00%)  | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                | 0               | 0               | 1               |
| <b>HYPOAESTHESIA</b>             |                 |                 |                 |
| subjects affected / exposed      | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 0               | 1               | 0               |
| <b>HYPOKINESIA</b>               |                 |                 |                 |
| subjects affected / exposed      | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 2 / 20 (10.00%) |
| occurrences (all)                | 0               | 1               | 2               |
| <b>NERVE COMPRESSION</b>         |                 |                 |                 |
| subjects affected / exposed      | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 1               | 0               | 0               |
| <b>ON AND OFF PHENOMENON</b>     |                 |                 |                 |
| subjects affected / exposed      | 1 / 20 (5.00%)  | 3 / 20 (15.00%) | 4 / 20 (20.00%) |
| occurrences (all)                | 1               | 3               | 4               |
| <b>PARAESTHESIA</b>              |                 |                 |                 |
| subjects affected / exposed      | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 0               | 1               | 0               |
| <b>POOR QUALITY SLEEP</b>        |                 |                 |                 |
| subjects affected / exposed      | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 0               | 1               | 0               |
| <b>PRESYNCOPE</b>                |                 |                 |                 |
| subjects affected / exposed      | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 0               | 1               | 0               |
| <b>PSYCHOMOTOR HYPERACTIVITY</b> |                 |                 |                 |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 20 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  |
| RESTING TREMOR<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| SCIATICA<br>subjects affected / exposed<br>occurrences (all)   | 0 / 20 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  |
| SOMNOLENCE<br>subjects affected / exposed<br>occurrences (all)   | 1 / 20 (5.00%)<br>1 | 3 / 20 (15.00%)<br>3 | 1 / 20 (5.00%)<br>2  |
| TREMOR<br>subjects affected / exposed<br>occurrences (all)   | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| VIBRATORY SENSE INCREASED<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| Ear and labyrinth disorders<br>TINNITUS<br>subjects affected / exposed<br>occurrences (all)            | 1 / 20 (5.00%)<br>1 | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0  |
| VERTIGO<br>subjects affected / exposed<br>occurrences (all)  | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Eye disorders<br>VISION BLURRED<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 20 (5.00%)<br>1 | 1 / 20 (5.00%)<br>1  | 2 / 20 (10.00%)<br>2 |
| VISUAL IMPAIRMENT<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 20 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  |
| Gastrointestinal disorders<br>ABDOMINAL PAIN UPPER<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| CONSTIPATION   |                     |                      |                      |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                   | 0 / 20 (0.00%) | 1 / 20 (5.00%)  | 1 / 20 (5.00%) |
| occurrences (all)                             | 0              | 1               | 1              |
| <b>DENTAL CARIES</b>                          |                |                 |                |
| subjects affected / exposed                   | 0 / 20 (0.00%) | 0 / 20 (0.00%)  | 1 / 20 (5.00%) |
| occurrences (all)                             | 0              | 0               | 1              |
| <b>DIARRHOEA</b>                              |                |                 |                |
| subjects affected / exposed                   | 0 / 20 (0.00%) | 0 / 20 (0.00%)  | 1 / 20 (5.00%) |
| occurrences (all)                             | 0              | 0               | 1              |
| <b>DYSPHAGIA</b>                              |                |                 |                |
| subjects affected / exposed                   | 0 / 20 (0.00%) | 0 / 20 (0.00%)  | 1 / 20 (5.00%) |
| occurrences (all)                             | 0              | 0               | 1              |
| <b>GASTRITIS</b>                              |                |                 |                |
| subjects affected / exposed                   | 1 / 20 (5.00%) | 0 / 20 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                             | 1              | 0               | 0              |
| <b>NAUSEA</b>                                 |                |                 |                |
| subjects affected / exposed                   | 0 / 20 (0.00%) | 2 / 20 (10.00%) | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 2               | 0              |
| <b>VOMITING</b>                               |                |                 |                |
| subjects affected / exposed                   | 0 / 20 (0.00%) | 1 / 20 (5.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 1               | 0              |
| <b>Skin and subcutaneous tissue disorders</b> |                |                 |                |
| <b>ERYTHEMA</b>                               |                |                 |                |
| subjects affected / exposed                   | 0 / 20 (0.00%) | 1 / 20 (5.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 1               | 0              |
| <b>NIGHT SWEATS</b>                           |                |                 |                |
| subjects affected / exposed                   | 0 / 20 (0.00%) | 0 / 20 (0.00%)  | 1 / 20 (5.00%) |
| occurrences (all)                             | 0              | 0               | 1              |
| <b>RASH</b>                                   |                |                 |                |
| subjects affected / exposed                   | 0 / 20 (0.00%) | 0 / 20 (0.00%)  | 1 / 20 (5.00%) |
| occurrences (all)                             | 0              | 0               | 1              |
| <b>Renal and urinary disorders</b>            |                |                 |                |
| <b>INCONTINENCE</b>                           |                |                 |                |
| subjects affected / exposed                   | 0 / 20 (0.00%) | 1 / 20 (5.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                             | 0              | 1               | 0              |
| <b>URGE INCONTINENCE</b>                      |                |                 |                |

|  |                 |                 |                |
|--|-----------------|-----------------|----------------|
| subjects affected / exposed                            | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                                      | 0               | 1               | 0              |
| <b>Musculoskeletal and connective tissue disorders</b> |                 |                 |                |
| <b>ARTHRALGIA</b>                                      |                 |                 |                |
| subjects affected / exposed                            | 1 / 20 (5.00%)  | 2 / 20 (10.00%) | 0 / 20 (0.00%) |
| occurrences (all)                                      | 1               | 3               | 0              |
| <b>BACK PAIN</b>                                       |                 |                 |                |
| subjects affected / exposed                            | 2 / 20 (10.00%) | 1 / 20 (5.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                                      | 2               | 1               | 0              |
| <b>JOINT SWELLING</b>                                  |                 |                 |                |
| subjects affected / exposed                            | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                                      | 0               | 1               | 0              |
| <b>LUMBAR SPINAL STENOSIS</b>                          |                 |                 |                |
| subjects affected / exposed                            | 0 / 20 (0.00%)  | 0 / 20 (0.00%)  | 1 / 20 (5.00%) |
| occurrences (all)                                      | 0               | 0               | 1              |
| <b>MOBILITY DECREASED</b>                              |                 |                 |                |
| subjects affected / exposed                            | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                                      | 1               | 0               | 0              |
| <b>MUSCLE RIGIDITY</b>                                 |                 |                 |                |
| subjects affected / exposed                            | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                                      | 0               | 1               | 0              |
| <b>MUSCLE SPASMS</b>                                   |                 |                 |                |
| subjects affected / exposed                            | 1 / 20 (5.00%)  | 0 / 20 (0.00%)  | 1 / 20 (5.00%) |
| occurrences (all)                                      | 1               | 0               | 1              |
| <b>MUSCULOSKELETAL CHEST PAIN</b>                      |                 |                 |                |
| subjects affected / exposed                            | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                                      | 0               | 1               | 0              |
| <b>MUSCULOSKELETAL PAIN</b>                            |                 |                 |                |
| subjects affected / exposed                            | 1 / 20 (5.00%)  | 1 / 20 (5.00%)  | 0 / 20 (0.00%) |
| occurrences (all)                                      | 1               | 1               | 0              |
| <b>OSTEOARTHRITIS</b>                                  |                 |                 |                |
| subjects affected / exposed                            | 0 / 20 (0.00%)  | 1 / 20 (5.00%)  | 1 / 20 (5.00%) |
| occurrences (all)                                      | 0               | 1               | 1              |
| <b>PAIN IN EXTREMITY</b>                               |                 |                 |                |

|  |                      |                     |                      |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                   | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  |
| <b>POLYARTHRITIS</b><br>subjects affected / exposed<br>occurrences (all)           | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  |
| <b>Infections and infestations</b>   |                      |                     |                      |
| <b>EAR INFECTION</b><br>subjects affected / exposed<br>occurrences (all)           | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  |
| <b>NASOPHARYNGITIS</b><br>subjects affected / exposed<br>occurrences (all)         | 2 / 20 (10.00%)<br>2 | 1 / 20 (5.00%)<br>1 | 2 / 20 (10.00%)<br>2 |
| <b>PURULENT DISCHARGE</b><br>subjects affected / exposed<br>occurrences (all)      | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  |
| <b>RHINITIS</b><br>subjects affected / exposed<br>occurrences (all)                | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  |
| <b>TOOTH ABSCESS</b><br>subjects affected / exposed<br>occurrences (all)           | 0 / 20 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  |
| <b>URINARY TRACT INFECTION</b><br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>2  | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  |
| <b>Metabolism and nutrition disorders</b>  |                      |                     |                      |
| <b>DEHYDRATION</b><br>subjects affected / exposed<br>occurrences (all)             | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0  |
| <b>GOUT</b><br>subjects affected / exposed<br>occurrences (all)                    | 0 / 20 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 20 (0.00%)<br>0  |
| <b>HYPERCHOLESTEROLAEMIA</b><br>subjects affected / exposed<br>occurrences (all)   | 1 / 20 (5.00%)<br>1  | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1  |
| <b>HYPOCALCAEMIA</b>   |                      |                     |                      |

|                               |                |                |                |
|-------------------------------|----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)             | 0              | 0              | 1              |
| <b>HYPONATRAEMIA</b>          |                |                |                |
| subjects affected / exposed   | 0 / 20 (0.00%) | 1 / 20 (5.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 1              | 0              |
| <b>INCREASED APPETITE</b>     |                |                |                |
| subjects affected / exposed   | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)             | 0              | 0              | 1              |
| <b>VITAMIN B12 DEFICIENCY</b> |                |                |                |
| subjects affected / exposed   | 1 / 20 (5.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 1              | 0              | 0              |

|   |                  |  |  |
|---|------------------|--|--|
| <b>Non-serious adverse events</b>                     | AFQ056 100 MG    |  |  |
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 46 / 69 (66.67%) |  |  |
| <b>Vascular disorders</b>                             |                  |  |  |
| <b>CIRCULATORY COLLAPSE</b>                           |                  |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%)   |  |  |
| occurrences (all)                                     | 0                |  |  |
| <b>DEEP VEIN THROMBOSIS</b>                           |                  |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%)   |  |  |
| occurrences (all)                                     | 0                |  |  |
| <b>HYPERTENSION</b>                                   |                  |  |  |
| subjects affected / exposed                           | 1 / 69 (1.45%)   |  |  |
| occurrences (all)                                     | 1                |  |  |
| <b>HYPOTENSION</b>                                    |                  |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%)   |  |  |
| occurrences (all)                                     | 0                |  |  |
| <b>ORTHOSTATIC HYPOTENSION</b>                        |                  |  |  |
| subjects affected / exposed                           | 2 / 69 (2.90%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| <b>RAYNAUD'S PHENOMENON</b>                           |                  |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%)   |  |  |
| occurrences (all)                                     | 0                |  |  |
| <b>THROMBOPHLEBITIS SUPERFICIAL</b>                   |                  |  |  |

|   |                     |  |  |
|---|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| General disorders and administration<br>site conditions |                     |  |  |
| ASTHENIA  |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| DEVICE DISLOCATION                                      |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| FATIGUE   |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| GAIT DISTURBANCE  |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| NON-CARDIAC CHEST PAIN                                  |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| OEDEMA PERIPHERAL                                       |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| PYREXIA   |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| Respiratory, thoracic and mediastinal<br>disorders      |                     |  |  |
| DYSPHONIA   |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| DYSPNOEA  |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| PULMONARY ARTERIAL<br>HYPERTENSION                      |                     |  |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 69 (0.00%)<br>0 |  |  |
| PULMONARY EMBOLISM                                      |                     |  |  |

|                                |                |  |  |
|--------------------------------|----------------|--|--|
| subjects affected / exposed    | 0 / 69 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| <b>RESPIRATORY DISTRESS</b>    |                |  |  |
| subjects affected / exposed    | 0 / 69 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| <b>Psychiatric disorders</b>   |                |  |  |
| <b>ABNORMAL DREAMS</b>         |                |  |  |
| subjects affected / exposed    | 2 / 69 (2.90%) |  |  |
| occurrences (all)              | 2              |  |  |
| <b>ANXIETY</b>                 |                |  |  |
| subjects affected / exposed    | 1 / 69 (1.45%) |  |  |
| occurrences (all)              | 1              |  |  |
| <b>APATHY</b>                  |                |  |  |
| subjects affected / exposed    | 0 / 69 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| <b>COMPULSIVE SHOPPING</b>     |                |  |  |
| subjects affected / exposed    | 0 / 69 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| <b>CONFUSIONAL STATE</b>       |                |  |  |
| subjects affected / exposed    | 2 / 69 (2.90%) |  |  |
| occurrences (all)              | 3              |  |  |
| <b>DELIRIUM</b>                |                |  |  |
| subjects affected / exposed    | 0 / 69 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| <b>DEPRESSED MOOD</b>          |                |  |  |
| subjects affected / exposed    | 0 / 69 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| <b>DEPRESSION</b>              |                |  |  |
| subjects affected / exposed    | 3 / 69 (4.35%) |  |  |
| occurrences (all)              | 3              |  |  |
| <b>HALLUCINATION, AUDITORY</b> |                |  |  |
| subjects affected / exposed    | 0 / 69 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| <b>HALLUCINATION, VISUAL</b>   |                |  |  |
| subjects affected / exposed    | 2 / 69 (2.90%) |  |  |
| occurrences (all)              | 2              |  |  |

|                                    |                |  |  |
|------------------------------------|----------------|--|--|
| ILLUSION                           |                |  |  |
| subjects affected / exposed        | 1 / 69 (1.45%) |  |  |
| occurrences (all)                  | 2              |  |  |
| INSOMNIA                           |                |  |  |
| subjects affected / exposed        | 4 / 69 (5.80%) |  |  |
| occurrences (all)                  | 4              |  |  |
| LIBIDO INCREASED                   |                |  |  |
| subjects affected / exposed        | 1 / 69 (1.45%) |  |  |
| occurrences (all)                  | 1              |  |  |
| NIGHTMARE                          |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| RAPID EYE MOVEMENTS SLEEP ABNORMAL |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| SLEEP DISORDER                     |                |  |  |
| subjects affected / exposed        | 1 / 69 (1.45%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Investigations                     |                |  |  |
| AMYLASE INCREASED                  |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| BLOOD PRESSURE INCREASED           |                |  |  |
| subjects affected / exposed        | 1 / 69 (1.45%) |  |  |
| occurrences (all)                  | 1              |  |  |
| BLOOD TRIGLYCERIDES INCREASED      |                |  |  |
| subjects affected / exposed        | 1 / 69 (1.45%) |  |  |
| occurrences (all)                  | 1              |  |  |
| CARDIAC MURMUR                     |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| HAEMATOOCRIT DECREASED             |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| HAEMOGLOBIN DECREASED              |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                           | 0 / 69 (0.00%) |  |  |
| occurrences (all)                                     | 0              |  |  |
| <b>RED BLOOD CELL COUNT DECREASED</b>                 |                |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%) |  |  |
| occurrences (all)                                     | 0              |  |  |
| <b>WEIGHT DECREASED</b>                               |                |  |  |
| subjects affected / exposed                           | 2 / 69 (2.90%) |  |  |
| occurrences (all)                                     | 2              |  |  |
| <b>Injury, poisoning and procedural complications</b> |                |  |  |
| <b>BONE CONTUSION</b>                                 |                |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%) |  |  |
| occurrences (all)                                     | 0              |  |  |
| <b>EXCORIATION</b>                                    |                |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%) |  |  |
| occurrences (all)                                     | 0              |  |  |
| <b>FALL</b>   |                |  |  |
| subjects affected / exposed                           | 6 / 69 (8.70%) |  |  |
| occurrences (all)                                     | 9              |  |  |
| <b>HAND FRACTURE</b>                                  |                |  |  |
| subjects affected / exposed                           | 1 / 69 (1.45%) |  |  |
| occurrences (all)                                     | 1              |  |  |
| <b>HEAD INJURY</b>                                    |                |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%) |  |  |
| occurrences (all)                                     | 0              |  |  |
| <b>PERIORBITAL HAEMATOMA</b>                          |                |  |  |
| subjects affected / exposed                           | 1 / 69 (1.45%) |  |  |
| occurrences (all)                                     | 1              |  |  |
| <b>THERMAL BURN</b>                                   |                |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%) |  |  |
| occurrences (all)                                     | 0              |  |  |
| <b>WOUND</b>  |                |  |  |
| subjects affected / exposed                           | 0 / 69 (0.00%) |  |  |
| occurrences (all)                                     | 0              |  |  |
| <b>Cardiac disorders</b>                              |                |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| CONDUCTION DISORDER         |                  |  |  |
| subjects affected / exposed | 0 / 69 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| DIASTOLIC DYSFUNCTION       |                  |  |  |
| subjects affected / exposed | 0 / 69 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| PALPITATIONS                |                  |  |  |
| subjects affected / exposed | 1 / 69 (1.45%)   |  |  |
| occurrences (all)           | 1                |  |  |
| <hr/>                       |                  |  |  |
| Nervous system disorders    |                  |  |  |
| AKINESIA                    |                  |  |  |
| subjects affected / exposed | 3 / 69 (4.35%)   |  |  |
| occurrences (all)           | 3                |  |  |
| BRADYKINESIA                |                  |  |  |
| subjects affected / exposed | 1 / 69 (1.45%)   |  |  |
| occurrences (all)           | 1                |  |  |
| COGNITIVE DISORDER          |                  |  |  |
| subjects affected / exposed | 0 / 69 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| DISTURBANCE IN ATTENTION    |                  |  |  |
| subjects affected / exposed | 0 / 69 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| DIZZINESS                   |                  |  |  |
| subjects affected / exposed | 6 / 69 (8.70%)   |  |  |
| occurrences (all)           | 11               |  |  |
| DYSKINESIA                  |                  |  |  |
| subjects affected / exposed | 13 / 69 (18.84%) |  |  |
| occurrences (all)           | 17               |  |  |
| FREEZING PHENOMENON         |                  |  |  |
| subjects affected / exposed | 0 / 69 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| HEADACHE                    |                  |  |  |
| subjects affected / exposed | 3 / 69 (4.35%)   |  |  |
| occurrences (all)           | 3                |  |  |
| HYPOAESTHESIA               |                  |  |  |

|                                  |                |  |  |
|----------------------------------|----------------|--|--|
| subjects affected / exposed      | 0 / 69 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| <b>HYPOKINESIA</b>               |                |  |  |
| subjects affected / exposed      | 0 / 69 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| <b>NERVE COMPRESSION</b>         |                |  |  |
| subjects affected / exposed      | 0 / 69 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| <b>ON AND OFF PHENOMENON</b>     |                |  |  |
| subjects affected / exposed      | 6 / 69 (8.70%) |  |  |
| occurrences (all)                | 7              |  |  |
| <b>PARAESTHESIA</b>              |                |  |  |
| subjects affected / exposed      | 2 / 69 (2.90%) |  |  |
| occurrences (all)                | 2              |  |  |
| <b>POOR QUALITY SLEEP</b>        |                |  |  |
| subjects affected / exposed      | 0 / 69 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| <b>PRESYNCOPE</b>                |                |  |  |
| subjects affected / exposed      | 0 / 69 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| <b>PSYCHOMOTOR HYPERACTIVITY</b> |                |  |  |
| subjects affected / exposed      | 0 / 69 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| <b>RESTING TREMOR</b>            |                |  |  |
| subjects affected / exposed      | 0 / 69 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| <b>SCIATICA</b>                  |                |  |  |
| subjects affected / exposed      | 0 / 69 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| <b>SOMNOLENCE</b>                |                |  |  |
| subjects affected / exposed      | 1 / 69 (1.45%) |  |  |
| occurrences (all)                | 1              |  |  |
| <b>TREMOR</b>                    |                |  |  |
| subjects affected / exposed      | 1 / 69 (1.45%) |  |  |
| occurrences (all)                | 2              |  |  |
| <b>VIBRATORY SENSE INCREASED</b> |                |  |  |

|  |                     |  |  |
|--|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 69 (0.00%)<br>0 |  |  |
| Ear and labyrinth disorders<br>TINNITUS<br>subjects affected / exposed<br>occurrences (all)            | 0 / 69 (0.00%)<br>0 |  |  |
| VERTIGO<br>subjects affected / exposed<br>occurrences (all)  | 1 / 69 (1.45%)<br>2 |  |  |
| Eye disorders<br>VISION BLURRED<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 69 (1.45%)<br>2 |  |  |
| VISUAL IMPAIRMENT<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 69 (1.45%)<br>1 |  |  |
| Gastrointestinal disorders<br>ABDOMINAL PAIN UPPER<br>subjects affected / exposed<br>occurrences (all) | 2 / 69 (2.90%)<br>2 |  |  |
| CONSTIPATION<br>subjects affected / exposed<br>occurrences (all)                                       | 5 / 69 (7.25%)<br>5 |  |  |
| DENTAL CARIES<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 69 (0.00%)<br>0 |  |  |
| DIARRHOEA<br>subjects affected / exposed<br>occurrences (all)  | 0 / 69 (0.00%)<br>0 |  |  |
| DYSPHAGIA<br>subjects affected / exposed<br>occurrences (all)  | 1 / 69 (1.45%)<br>1 |  |  |
| GASTRITIS<br>subjects affected / exposed<br>occurrences (all)  | 0 / 69 (0.00%)<br>0 |  |  |
| NAUSEA   |                     |  |  |

|   |   |  |  |
|---|---|--|--|
| <p>subjects affected / exposed<br/>occurrences (all)</p> <p>VOMITING</p> <p>subjects affected / exposed<br/>occurrences (all)</p>   | <p>3 / 69 (4.35%)<br/>3</p> <p>2 / 69 (2.90%)<br/>2</p>   |  |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>ERYTHEMA</p> <p>subjects affected / exposed<br/>occurrences (all)</p> <p>NIGHT SWEATS</p> <p>subjects affected / exposed<br/>occurrences (all)</p> <p>RASH</p> <p>subjects affected / exposed<br/>occurrences (all)</p>  | <p>0 / 69 (0.00%)<br/>0</p> <p>1 / 69 (1.45%)<br/>1</p> <p>1 / 69 (1.45%)<br/>1</p>                             |  |  |
| <p>Renal and urinary disorders</p> <p>INCONTINENCE</p> <p>subjects affected / exposed<br/>occurrences (all)</p> <p>URGE INCONTINENCE</p> <p>subjects affected / exposed<br/>occurrences (all)</p>   | <p>0 / 69 (0.00%)<br/>0</p> <p>0 / 69 (0.00%)<br/>0</p>   |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>ARTHRALGIA</p> <p>subjects affected / exposed<br/>occurrences (all)</p> <p>BACK PAIN</p> <p>subjects affected / exposed<br/>occurrences (all)</p> <p>JOINT SWELLING</p> <p>subjects affected / exposed<br/>occurrences (all)</p> <p>LUMBAR SPINAL STENOSIS</p> <p>subjects affected / exposed<br/>occurrences (all)</p> <p>MOBILITY DECREASED</p> | <p>2 / 69 (2.90%)<br/>2</p> <p>2 / 69 (2.90%)<br/>3</p> <p>0 / 69 (0.00%)<br/>0</p> <p>0 / 69 (0.00%)<br/>0</p> |  |  |

|                                    |                 |  |  |
|------------------------------------|-----------------|--|--|
| subjects affected / exposed        | 2 / 69 (2.90%)  |  |  |
| occurrences (all)                  | 2               |  |  |
| <b>MUSCLE RIGIDITY</b>             |                 |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%)  |  |  |
| occurrences (all)                  | 0               |  |  |
| <b>MUSCLE SPASMS</b>               |                 |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%)  |  |  |
| occurrences (all)                  | 0               |  |  |
| <b>MUSCULOSKELETAL CHEST PAIN</b>  |                 |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%)  |  |  |
| occurrences (all)                  | 0               |  |  |
| <b>MUSCULOSKELETAL PAIN</b>        |                 |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%)  |  |  |
| occurrences (all)                  | 0               |  |  |
| <b>OSTEOARTHRITIS</b>              |                 |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%)  |  |  |
| occurrences (all)                  | 0               |  |  |
| <b>PAIN IN EXTREMITY</b>           |                 |  |  |
| subjects affected / exposed        | 3 / 69 (4.35%)  |  |  |
| occurrences (all)                  | 3               |  |  |
| <b>POLYARTHRITIS</b>               |                 |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%)  |  |  |
| occurrences (all)                  | 0               |  |  |
| <b>Infections and infestations</b> |                 |  |  |
| <b>EAR INFECTION</b>               |                 |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%)  |  |  |
| occurrences (all)                  | 0               |  |  |
| <b>NASOPHARYNGITIS</b>             |                 |  |  |
| subjects affected / exposed        | 9 / 69 (13.04%) |  |  |
| occurrences (all)                  | 9               |  |  |
| <b>PURULENT DISCHARGE</b>          |                 |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%)  |  |  |
| occurrences (all)                  | 0               |  |  |
| <b>RHINITIS</b>                    |                 |  |  |
| subjects affected / exposed        | 1 / 69 (1.45%)  |  |  |
| occurrences (all)                  | 1               |  |  |

|                                    |                |  |  |
|------------------------------------|----------------|--|--|
| TOOTH ABSCESS                      |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| URINARY TRACT INFECTION            |                |  |  |
| subjects affected / exposed        | 4 / 69 (5.80%) |  |  |
| occurrences (all)                  | 6              |  |  |
| Metabolism and nutrition disorders |                |  |  |
| DEHYDRATION                        |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| GOUT                               |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| HYPERCHOLESTEROLAEMIA              |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| HYPOCALCAEMIA                      |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| HYPONATRAEMIA                      |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| INCREASED APPETITE                 |                |  |  |
| subjects affected / exposed        | 0 / 69 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| VITAMIN B12 DEFICIENCY             |                |  |  |
| subjects affected / exposed        | 1 / 69 (1.45%) |  |  |
| occurrences (all)                  | 1              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment  |
|--------------|--|
| 05 June 2012 | The protocol was amended to allow concomitant treatment with amantadine and to collect long-term safety and safety data on concomitant amantadine and AFQ056 in this patient population. Amantadine was frequently used to treat LIDs and permitting concomitant treatment with AFQ056 may provide additional treatment options for these patients. AEs associated with amantadine are similar to AFQ056 (e.g. dizziness, hallucinations, fatigue), and concomitant administration with AFQ056 may increase the likelihood of these AEs. However, these events were expected to be transient and reversible.<br>In addition, the amended protocol, in line with the FDA Guidance on the prospective suicidality assessment in clinical trials, required the C-SSRS to be assessed at every postbaseline visit, including unscheduled visits. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

|  |
|--|
| The study was terminated based on the results of studies CAFQ056A2222 and CAFQ056A2223 (due to lack of efficacy) and the sponsor's decision to terminate the program |
|--|

Notes: