### 1. Trial information:

<table>
<thead>
<tr>
<th>Field</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject ID</td>
<td></td>
</tr>
<tr>
<td>Site No.</td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td></td>
</tr>
<tr>
<td>If blinded trial, was the study treatment unblinded?</td>
<td>Yes [ ] No [ ]</td>
</tr>
<tr>
<td>Is this the initial report of an SAE or a follow-up?</td>
<td>Initial [ ] Follow-up, follow up no. [ ]</td>
</tr>
</tbody>
</table>

**In which period of the trial is the subject currently enrolled?**

- [ ] Screening and initial treatment
- [ ] Maintenance treatment
- [ ] Extended follow up
- [ ] Open-label treatment
- [ ] Short-term extension

### 2. Subject details:

<table>
<thead>
<tr>
<th>Field</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (at time of event onset) or date of birth (DD-MM-YYYY):</td>
<td></td>
</tr>
<tr>
<td>Weight (kg):</td>
<td></td>
</tr>
<tr>
<td>Height (cm):</td>
<td></td>
</tr>
</tbody>
</table>

-  Male [ ]
-  Female [ ]

To report a pregnancy case, please complete a Pregnancy Reporting Form.

### 3. Adverse event meets the following criteria for being serious:

-  Death [ ]
-  Life-threatening [ ]
-  In-patient hospitalisation/ Prolongation of existing hospitalisation [ ]
-  Persistent or significant disability/incapacity [ ]
-  A congenital anomaly/birth defect [ ]
-  Other medically important condition [ ]

### 4. When did the event meet the criteria for being serious?

(DD-MM-YYYY)

### 5. When did any trial staff first become aware of the event?

(DD-MM-YYYY)

### 6. If the subject has been hospitalised for the event, please fill in:

-  Date of hospitalisation:  (DD-MM-YYYY)
-  Date of discharge:  (DD-MM-YYYY)

### 7. Was the subject withdrawn from the trial due to this SAE?

-  No [ ]
-  Yes [ ]

### 8. Description of SAE: (Diagnosis, signs, symptoms, course of event, drugs used for treatment and examinations/treatments performed)

Instructions for completion on page 5
9. Please record main diagnosis or provisional diagnosis (alternatively symptom) for this medical episode.
If the subject experienced diagnoses with different onset or stop time, different severity, outcome or causality, please specify for each.

<table>
<thead>
<tr>
<th>Serious Adverse Event</th>
<th>Outcome</th>
<th>Severity</th>
<th>Causality towards the investigational product</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recovered/Resolved</td>
<td></td>
<td>Probable</td>
</tr>
<tr>
<td></td>
<td>Recovering/Resolving</td>
<td></td>
<td>Possible</td>
</tr>
<tr>
<td></td>
<td>Not recovered/Not resolved</td>
<td></td>
<td>Not related</td>
</tr>
<tr>
<td></td>
<td>Recovered with sequelae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fatal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Was this SAE related to a Product Quality Complaint? No ☐ Yes ☐
If yes, please specify

If the SAE resolved with sequelae, specify sequelae:

If fatal, what was immediate cause of death: Autopsy performed? No ☐ Yes ☐
(please attach report)

Is the SAE suspected to be causally related to any of the following, please specify
☐ Non-investigational product, e.g. rescue medication
☐ Trial related procedure, e.g. screening procedure or diagnostic test
☐ Non-trial related cause, e.g. trauma
Serious Adverse Event (SAE) Form – Clinical Trials

Protocol Code number: LP0162-1325

10. Investigational product

<table>
<thead>
<tr>
<th>Investigational product</th>
<th>Dose + Frequency OR Total Daily Dose (specify dose units)</th>
<th>Route (e.g. oral, IV, topical, etc.)</th>
<th>Duration of therapy (DD-MMM-YYYY)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Started</td>
<td>Stopped</td>
</tr>
</tbody>
</table>

Did the subject use any rescue treatment? ☐ Yes ☐ No
If yes, please specify the indication
If yes, please specify the drug and treatment dates

11. Dechallenge/Rechallenge

a. Was investigational product stopped? ☐ Yes ☐ No ☐ N/A
b. Was investigational product stopped due to SAE? ☐ Yes ☐ No ☐ N/A
   If no, specify other reason for stopping:

c. Did the SAE disappear after investigational product was stopped? ☐ Yes ☐ No ☐ N/A
d. Did the SAE reappear after restart of investigational product? ☐ Yes ☐ No ☐ N/A
e. Was the per protocol dose regimen changed? ☐ Yes ☐ No ☐ N/A
   If yes, specify action taken:

12. Concomitant medication (exclude drugs given to treat events as these must be recorded in the SAE description (section 8)). ☐ None ☐ Attached (CRF can be attached)

<table>
<thead>
<tr>
<th>Drug(s) (trade name or generic name)</th>
<th>Formulation and strength (e.g. tab 5 mg)</th>
<th>Dose + Frequency OR Total Daily Dose (dose units)</th>
<th>Route (e.g. oral, IV, topical)</th>
<th>Duration of therapy (DD-MMM-YYYY)</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Started</td>
<td>Stopped</td>
</tr>
</tbody>
</table>

13. Are any of the concomitant medications suspected of being causally related to the SAE? ☐ Yes ☐ No
   If yes, please specify drug
   Did the SAE disappear after stop of drug? ☐ Yes ☐ No ☐ N/A
   Did the SAE reappear after restart of drug? ☐ Yes ☐ No ☐ N/A

Instructions for completion on page 7
### 14. Subject’s medical history

- **None**

  If more space is required, use another SAE form.

<table>
<thead>
<tr>
<th>Disease, surgical procedure, etc.</th>
<th>Start date</th>
<th>End date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>

### 15. Subject’s relevant current medical conditions

- **None**

<table>
<thead>
<tr>
<th>Disease, surgical procedure, etc.</th>
<th>Start date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
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</tr>
</tbody>
</table>

### 16. SAE-relevant clinical/laboratory assessments

- **None**

  - Attached

<table>
<thead>
<tr>
<th>Test</th>
<th>Assessment date (DD-MMM-YYYY)</th>
<th>Result</th>
<th>Unit (SI)</th>
<th>Reference interval</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>

### 17. Reporter details

- **(Sub)-Investigator’s name**
- **Signature**
- **Date (DD-MMM-YYYY)**

  If Reporter other than (Sub)-Investigator please state:

- **Reporter’s name**
- **Signature**
- **Date (DD-MMM-YYYY)**

---

**For LEO internal use only**

Date LEO was first notified

**Signature**
Serious Adverse Event (SAE) Form – Clinical Trials

Instructions for completion

General instructions to be found at the bottom of page 8

1. Trial information
   - Enter LEO Protocol Code No, subject ID and Site No. Enter country in which SAE took place.
   - Study treatment must only be unblinded by the investigator in an emergency where investigational product identification is necessary.
   - Tick Initial or Follow-up report and indicate the number of follow-up report (1, 2, 3,…).

2. Subject details
   - Age (at time of event onset) and/or Date of birth and all other dates should be stated as DD-MMM-YYYY.
   - For pregnant subjects experiencing one or more SAEs this form is used.
   - The SAE form should NOT be used to collect observations of pregnancy. Pregnancy observations should be recorded in a Pregnancy Reporting Form.

3. Criteria for making the adverse event serious
   A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose meets any of the following conditions, please tick the appropriate
   - Death – the outcome of the SAE was fatal;
   - Life-threatening – at risk of death at the time of the SAE (not an event that hypothetically might have caused death if more severe);
   - In-patient hospitalisation – admission to hospital for at least 24 hours as a result of the SAE (hospitalisation for logistic/convenience reasons or for trial-related purposes are not untoward medical occurrences and therefore are not an SAE); or Prolongation of existing hospitalisation – in-patient hospitalisation extended;
   - Persistent or significant disability/incapacity – significant/persistent/permanent change in subject’s body function, quality of life or in limitations of physical or working abilities;
   - A congenital anomaly/birth defect – SAE potentially caused by exposure to investigational product prior to conception or during pregnancy;
   - Other medically important condition – Events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed above. Examples of such events are allergic bronchospasm, blood dyscrasias, convulsions or suspected transmission of an infectious agent via the investigational product.

4. The date when the adverse event became serious
   Symptoms of the SAE may have started prior to this date but the date when the event is fulfilling the seriousness criteria is the correct date to be recorded.

5. The date when the any study staff first became aware of the event
   Symptoms of the SAE may have started prior to this date.

6. Dates of admission and discharge from hospital
   Only relevant if the subject is hospitalised for the SAE.

7. Subject withdrawn from the trial due to this SAE
   Tick Yes if the subject was withdrawn from the trial due to the SAE even if the SAE is not related to investigational product.
   Tick No if subject remains in the trial.

8. Detailed description of the SAE
   Provide a chronological description using standard medical terminology of the event including diagnosis/provisional diagnosis, signs, symptoms, course of event, drugs used for treatment of the event, and other examinations (e.g. CT scan) or treatments performed. Use this space for other comments about the SAE that you may like to add. If more space is required, use another SAE form.
Instructions for completion

9. Main diagnosis or provisional diagnosis (alternatively symptom) for this medical episode
Preferably one main diagnosis (if known) rather than sign/symptom of this medical episode should be given.
Should the medical episode consist of more than one serious adverse event, please complete a copy of this page for each serious event.

Serious Adverse Event – state diagnosis/provisional diagnosis of the SAE described in precise, standard medical terminology.
Do not enter "Hospitalisation" or "Death" as SAE, as hospitalisation is a criteria for the event being serious and death is an outcome.

Start date – First day with any adverse symptoms, or a clear deterioration of a pre-existing condition. For example, the onset of an event may occur before a hospitalisation.

Stop date – The day where adverse event symptoms have resolved or simply a return to baseline conditions (stop date is not necessarily the date of discharge from hospital).

Outcome
- Recovered/resolved: The event has stopped. The stop date of the event must be recorded.
- Recovering/resolving: The subject is clearly recovering from an event. The event is, however, not yet completely resolved. Follow-up on the event is required (by sending a follow-up SAE Form) until final outcome is established. The SAE stop date should be left blank.
- Not recovered/not resolved: Event is still ongoing. Follow-up on the event is required until final outcome is established. The SAE stop date should be left blank.
- Recovered with sequelae: The event has reached a state where no further changes are expected and the residual symptoms are assumed to persist. An example is hemiparesis after stroke. Record SAE stop date and specify the sequelae below the table.
- Fatal: The subject has died as a consequence of the event. Date of death is recorded as stop date of the adverse event. The immediate cause of death should be recorded below the table.
- Unknown: Unknown to Investigator, e.g. subject lost to follow-up. The SAE stop date should be left blank.

Severity – Describe the intensity of the event as mild, moderate or severe.
Mild: An AE that is usually transient and may require only minimal treatment or therapeutic intervention. The event does not generally interfere with usual activities of daily living.
Moderate: An AE that is usually alleviated with additional specific therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk or harm to the subject.
Severe: An AE that interrupts usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention.

Causality – assessment of the relationship between the investigational product(s) and the SAE must always be made or confirmed by the (Sub)-Investigator.
Probable: the SAE
- follows a reasonable temporal sequence from administration of the investigational product.
- could not be reasonably explained by the subject’s clinical state, environmental or toxic factors or other therapies administered to the subject.
- follows a known pattern of response to the investigational product.
- disappears or decreases on cessation or reduction in dose of the investigational product.
- reappears or worsens upon re-challenge.

Possible: the SAE
- follows a reasonable temporal sequence from administration of the investigational product.
- Could also be reasonably explained by the subject’s clinical state, environmental or toxic factors or other therapies administered to the subject.
- follows a known pattern of response to the investigational product.

Not related: the SAE
- does not follow a reasonable temporal sequence from administration of the investigational product.
- is better explained by other factor like the subject’s clinical state, the environmental or toxic factors or other therapies administered to the subject.
- does not reappear or worsen upon re-challenge.
- does not follow a known pattern of response to the investigational product.

If fatal – Provide date of death, cause of death and autopsy report (if available).
Instructions for completion

10. Investigational product
   - Name as stated in the protocol
   - State “Blinded” if blinded trial and treatment has not been unblinded
   - State “No drug” if subject never received investigational product (e.g. during wash-out)

   Dose + Frequency OR - e.g. 5 mg TID OR
   Total Daily Dose - e.g. 15 mg
   Route - Written form (e.g. oral) or short form (e.g. PO)
   Duration of therapy - State start and stop dates for treatment
   - State “Ongoing” if subject is still administered investigational product

   If the subject received rescue treatment please specify and provide the indication.

11. Dechallenge/Rechallenge
   • Answer all questions a-e.
   • Tick N/A in all cases where the question does not apply.
   • e) If the per protocol dose regimen was changed specify action (e.g. dose changed as per protocol, investigational product temporarily stopped/permanently stopped).

12. Concomitant medication
   • Tick "None" if no concomitant medication to verify that the table should be left blank.
   • Tick "Attached" if the CRF has the same information and is attached
   • Include current medications used and medications taken within 30 days prior to the SAE.
   • Do not include medications used to treat the SAE. Such medications should be mentioned in section 8 (Description of the SAE).
   • Data should be entered by the same convention as for section 10.

13. Are any of the concomitant medications suspected to be causally related to the SAE?
   Please give as many details as possible about other drugs suspected to have caused the SAE(s). Specify which drug is suspected to have caused which SAE.

14. Subject’s Medical History
   • Tick "None" if no medical history to verify that the table should be left blank
   • Specify medical history
   • Provide Start and End dates if available (approximations acceptable).
     If Start date or End date is unknown enter UNK (Unknown).
   • Comments can be written in the last column if required.

15. Subject’s relevant current medical conditions
   • Tick "None" if no relevant current medical conditions to verify that the table should be left blank.
   • Specify relevant current medical conditions.
   • Provide Start date if available (approximations acceptable).
     If Start date is unknown enter UNK (Unknown).
   • Comments can be written in the last column if required.

16. SAE- relevant clinical/Laboratory assessments
   • Tick "None" if no assessments to verify that the table should be left blank.
   • Lab results can be attached or entered into the table. Tick "Attached" and/or “See below” as relevant.
   • Test - Name of the test.
   • Assessment Date - Date of the assessment
   • Result - The value of the result.
   • Unit - The SI unit of the result (International System of Units).
   • Ensure to provide the reference range

17. Reporter details – The (Sub)-Investigator must sign and date the SAE report
   The (Sub)-Investigator must sign and date the report which acknowledges his/her awareness of the event and that he/she made the assessment of the causal relationship of the investigational product(s) and any of the other medications to the SAE(s).

   The actual reporter, if not the (Sub)-Investigator should also sign and date the report.

   For LEO internal use only – (Sub-)Investigator should not complete this area.
General Instructions

- Use black or blue ink or type (reports must remain legible when faxed).
- If additional space is required, use another SAE Form.
- Dates must be entered as DD-MMM-YYYY e.g. 11-MAR-2011.
  - if day is unknown, use XX (e.g. XX-MAR-2011).
- On pages 1 and 2, enter CRF No. in top right corner.

SAEs should be collected from the time of the signing of the Informed Consent Form, whether or not the subject has received investigational product, and until the timeline specified in the protocol.

WITHIN 24 hours of first knowledge by any trial staff, all SAEs related or unrelated to investigational product must be reported to LEO Pharma or LEO Pharma representative as per trial agreement using this SAE Form.

Fax: +45 72 26 32 87
E-mail: drug.safety@leo-pharma.com

All SAEs must also be recorded in the CRF.

Follow-up Reports
When a SAE follow-up is reported, a new SAE form should be completed. If there is no new information to add to the narrative, drug therapy or concomitant medication sections, “See Initial Report” or “N/A” may be stated in these fields.

Updates to the eCRF with regards to the reported term, SAE onset date/stop dates and outcome of the SAE should be reported to GPV via the SAE form and vice versa.

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