

SERIOUS ADVERSE EVENT REPORT INSTRUCTIONS

Instructions for completion of the form:

When to fill out the HOVON Serious Adverse Event Report

Fill out the report if a patient included in a HOVON trial experiences a Serious Adverse Event (SAE) during the trial. Report all SAE's that occur from the first trial related procedure or treatment until 30 days after the last dose of protocol treatment. For definitions and trial specific conditions please refer to the trial protocol. Any SAE should be reported to the HOVON Data Center within 24 hours.

Who should fill out the HOVON Serious Adverse Event Report

Any authorized member of the site trial staff may fill out the report; this can be a (sub-) investigator, research nurse, data manager or other qualified person. However, the investigator (or sub-investigator) is responsible for the SAE report and should review the medical content of the form and sign the final report.

How to complete the HOVON Serious Adverse Event Report

Fill out all applicable items. Detailed instructions are listed below. Fill out a separate form for each Serious Adverse Event. Always send in all 3 pages of the form. Please complete the form in English.

Each SAE report is identified by a set of items that must always be filled out for each report and repeated on every page of the report: Patient study number, Patient namecode, Date of report, type of report.

Patient study number: number that was assigned by the HOVON Data Center to the patient at registration/randomization;

Patient namecode: patient initials or namecode as reported at registration/randomization;

Date of report: as reported on the first page of the form;

Type of report: initial, follow up or final report; mark the applicable box.

Corrections and new information

Make corrections by crossing out the incorrect answer once (do not obscure the original entry) and writing the new answer next to it, dated, initialed, and explained (if necessary). Do not use correction tape or fluid. When sending in a corrected copy of a report that was sent earlier, please make sure that it is clearly marked as a correction.

New information can be added when sending in a follow up or final report (see below). Use the existing SAE form and simply add the new information to the form or make corrections as described above.

Avoid using a new blank form to send in corrections or new information on a previously reported SAE. However, there may be a reason why this is necessary, for example if you need to send more than 3 follow up reports. If you are using a new blank form, copy all items in "Report information" and "Serious Adverse Event information" from the previous report (initial or follow up) to the new report (follow up or final). If you use a new form for the follow up or final report, make sure that the information does not contradict the information on the previous report.

Initial report

The initial report must be sent to the HOVON Data Center within 24 hours. It should contain a minimum amount of information:

Patient information: Patient study number, Patient namecode, Date of birth;

Report information: Site name, Investigator, Type of report (mark "initial report"), Date of initial report;

Serious Adverse Event information: all items;

Trial medication: Treatment arm and Protocol phase, Trial medication name and Relationship to SAE;

Additional SAE information: if applicable, other Location and Date investigator was aware of the SAE;

Signatures: all items for initial report.

Follow up report

A first follow up report must be sent to the HOVON Data center within 2 working days after the initial report was sent if not all information regarding the SAE could be completed in the initial report. Send in follow up reports at least once every month thereafter until a final report can be completed.

The first follow up report should contain all information regarding the SAE as available at that time:

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Patient information: all items;
Report information: Site name, Investigator, Type of report (mark "follow up report"), Date of follow up report;
Serious Adverse Event information: all items;
SAE description and comments: all relevant information as available at that time;
Trial medication: all items;
Concomitant medication: all items;
Relevant medical history: all relevant information;
Additional SAE information: all applicable information as available at that time;
Signatures: all items for follow up report.

Please make sure that a new Date of follow up report is filled out for each new follow up report. If you need to complete more than 3 follow up reports, continue on a new blank SAE form as described for "Corrections and new information".

Final report

A final report must be sent to the HOVON Data Center as soon as the outcome of the SAE is known. Every SAE must have a final report. The final report should contain all information regarding the SAE:

Patient information: all items;
Report information: Site name, Investigator, Type of report (mark "final report"), Date of final report;
Serious Adverse Event information: all items;
SAE description and comments: complete information;
Trial medication: all items;
Concomitant medication: all items;
Relevant medical history: all relevant information;
Additional SAE information: all applicable information, always include Outcome of SAE;
Signatures: all items for final report, the final report should always be signed by the (sub) investigator.

Instructions for completion of specific items:

Patient information

Patient study number: number that was assigned by the HOVON Data Center to the patient at registration/randomization
Patient namecode: patient initials or namecode as reported at registration/randomization

Report information

Site name: name of the hospital that is reporting the SAE;
Investigator: name of local investigator for that hospital;
Type of report: mark the applicable box. Every SAE must have at least an initial report and a final report. The initial report may already contain all the information required for the final report - mark the boxes for "initial report" and "final report" with identical Date of initial report and Date of final report. A follow up report is required within 2 business days after the initial report was sent if not all information regarding the SAE could be completed in the initial report, and once a month thereafter until the final report can be completed;
Date of report: the date the report (initial, follow up or final) was filled out. Please make sure that a new Date of follow up report is filled out for each new follow up report.

Serious Adverse Event information

Adverse Event term: the most precise diagnosis available for the event as assessed by the investigator or treating physician; this should be a single term (for example "sepsis" or "pulmonary embolism") and not an elaborate description. Preferably use terms from the NCI Common Terminology Criteria for Adverse events and use the same term when reporting the event on the Adverse Event CRF. If no diagnosis is available (yet), provide the most relevant sign or symptom (for example "fever" or "dyspnea");
Date onset AE: date the Adverse Event started, regardless whether it was already Serious at that time;
Date AE became Serious: date that the AE first matched the criteria for being a SAE, this can be the same date as *Date onset AE* or later;
Reason AE is Serious: if the AE matches more than one criterium, choose the most relevant.

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SAE description and comments

Use this box to describe the course of events from onset AE until end of the SAE. Include dates and results of any relevant tests or procedures that were used to diagnose the SAE, and actions taken to treat the SAE. Please note that some dates and actions are already described elsewhere in the form (dates of hospitalization, date of death, actions regarding trial medication).

Trial medication

Describe the medication that is part of the protocol treatment schedule and that the patient was receiving at the onset of the Adverse Event or shortly before that. Drugs that are used for supportive care or prophylaxis as recommended by the protocol (for example antibiotics), are not to be regarded as trial medication but as concomitant medication (see below).

Treatment arm: for randomized trials, enter the treatment arm the patient is treated in – should this for some reason be different from the arm the patient was assigned to at randomization, explain the discrepancy in the SAE description;

Protocol phase: enter the protocol phase during or after which the Adverse Event started;

Trial medication: enter all medications that the patient received during the protocol phase that the SAE is associated with, choose from the listed trial medications;

Date first dose: date the patient received the first dose of this trial medication as part of the associated protocol phase - so if the SAE started during cycle 2 and the patient already received this drug in cycle 1, use the start date from cycle 2;

Date last dose: date the patient received the last dose of this trial medication until the date the SAE started - this date must be before or the same as *Date AE became Serious*, regardless if the drug was continued after this date or not;

Relationship to SAE: assessment of the (sub) investigator for the causal relationship between the Adverse Event and the trial medication;

Action taken: action taken regarding the trial medication as a consequence of the Adverse Event;

Did event abate: if the trial medication was discontinued (temporarily or permanently), did the Adverse Event disappear or become less severe as a result?

Did event reappear: if the trial medication was restarted after the Adverse Event abated, did the AE reappear or become more severe again as a result?

Concomitant medication

Describe any medication that is not trial medication and that the patient was receiving at the onset of the Adverse Event or shortly before that. Do not include medication that was used to treat the Serious Adverse Event; this can be described as part of the *SAE description and comments*.

If the space provided on the form is not sufficient, report further concomitant medication on a separate page attached to the report. Indicate clearly on the SAE report that there is an attachment and indicate clearly on the attachment to which SAE report it belongs.

Indication: give the reason or diagnosis for which the concomitant medication was prescribed (for example "prophylaxis" or "hypertension");

Date first dose: date the patient received the first dose of this drug as part of the current treatment; this date should always be before *Date AE became Serious*;

Date last dose: date the patient received the last dose of this drug until the date the SAE started - this date must be before or the same as *Date AE became Serious*, regardless if the drug was continued after this date or not.

Relevant medical history

Use this box to describe any background information regarding the patient that may be relevant for this SAE, like concomitant diseases, allergies, if the patient experienced a similar event before, any other circumstances that may have contributed to the SAE (for example a fall down the stairs a few days earlier in case of a spontaneous bone fracture, a catheter that was inserted a few weeks earlier in case of an infection).

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Additional SAE information

Outcome of SAE:

- "resolved completely" the Adverse Event is no longer present
- "resolved with sequelae" the Adverse Event is resolved but there are still some residual problems as a result from the AE (for example restricted mobility after a CVA)
- "ongoing" the Adverse Event is still present – regardless of changes in severity
- "death" the Adverse Event is the (suspected) cause of death
- "ongoing at death" the Adverse Event was not yet resolved when the patient died from another cause: the Adverse Event is definitely not the cause of death

Please note that on a final report the SAE outcome cannot be "ongoing", unless the SAE is a significant/persistent disability or a congenital anomaly/birth defect.

Date SAE resolved: date the Adverse Event ended ("resolved completely" or "resolved with sequelae")

If patient was hospitalized: fill out these dates if the patient was hospitalized at any time during the course of the SAE, regardless if the *Reason AE is Serious* is (prolongation of) hospitalization or not. Also fill out these dates if the SAE occurred while the patient was already hospitalized for another reason (include that reason in the *SAE description and comments*).

If patient died: fill out these items if "death" was the reason for or the outcome of the SAE, or if the patient died from another cause while the SAE was still ongoing. Please note that if the patient died from another cause the cause of death is an SAE in itself and needs to be reported as such.

If the SAE onset was at another location: fill out these items if the SAE started at another location than the investigational site and the (sub) investigator became aware of the SAE at a later time (for example, the patient was admitted to another hospital for an emergency or died at home, and the investigator was informed by a letter of discharge or by a call from the general physician).

Signatures

The reporter responsible for the content of the SAE report should sign each report. The (sub) investigator should always sign the final report.

Instructions for sending and filing the form:

After completing the report, fax it to the HOVON Data Center; use the fax number printed in the header of the form.

Keep the original report at the site in a safe place where it can be easily accessed for further processing and monitoring (for example in the Investigator Trial File or a specific SAE Report File, with a copy stored in the patient file for reference by the treating physician and data manager).

Questions:

For questions regarding SAE reports you can contact the HOVON Data Center.

Telephone: +31 (0)10 70 41 560

E-mail: hdc@erasmusmc.nl (do not use for urgent questions)