SERIOUS ADVERSE EVENT REPORT

INSTRUCTIONS

Instructions for sending and filing the form:

After completing the report, fax or email it to the Clinical Trial Center by using the fax number or email (sae.invent.ctc@erasmusmc.nl) printed in the header of the form.

Please 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 File behind tab E2.6 or a specific SAE Report File, with a copy stored in the patient file for reference by the treating physician and data manager).

Signatures
The reporter responsible for the content of the SAE report should sign each report. The (sub) investigator or his/her delegate should always sign the final report. The Principle Investigator (or sub-investigator) remains responsible for the SAE report and should review the medical content of the form, sign at least the final report and report the SAE to the authorities (ToetsingOnline).

Questions:

Please contact us at appic@erasmusmc.nl if there are any questions.

Instructions for completion of the form:

When to fill out the APPIC Serious Adverse Event (SAE) Report
Please fill out an SAE report when a patient included in the APPIC trial experiences a Serious Adverse Event (SAE) during the trial. Please see www.appictrial.nl/sae-melding or section 9.2.2 of the protocol for a reference of which events are considered SAE's and which are an exception. Any SAE should be reported to the Clinical Trial Center within 24 hours.

Who should fill out the APPIC 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 at least the final report.

How to complete the APPIC Serious Adverse Event Report
Please fill out all applicable items, detailed instructions are listed below. Please fill out a separate form for each unique Serious Adverse Event. Always send in both 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*: number that was assigned to the patient at registration;
- *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
Corrections can be made by striking through the incorrect information once, such that the original entry is still readable and write the new information next to it, along with your initials and the date of correction and (if necessary) an explanation. 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 revision.

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.

Please avoid using a new blank form to send in corrections or new information on a previously sent 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 needed for identification; patient study number, year of birth, adverse event term, date onset AE and date AE became Serious 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
Please send the initial report to the Clinical Trial Center within 24 hours after the SAE occurred or after the investigator became aware of the SAE. The report should preferably contain all information that is known at the time of completion but the following items are mandatory:

- *Patient information*
- *Report information*
- *Serious Adverse Event information*
- *Signature*

If not all information (except for the mandatory items) regarding the SAE could be completed in the initial report, a complete report must be sent to the Clinical Trial Center as a follow up report within 2 working days after the initial report was sent. The complete report should contain all available information regarding the SAE at that time.

Follow up report
Please send in follow up reports at least once every month until a final report could be completed. Update the information as applicable in each 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 in the paragraph "Corrections and new information".

Final report
Please send a final report to the Clinical Trial Center as soon as the outcome of the SAE is known. Please note that every SAE must have a final report. The final report should contain all information regarding the SAE. The final report should always be signed by the (sub) investigator.

Instructions for completion of specific items:

Patient information

Patient study number:	unique number that was assigned to the patient at registration
Year of birth:	Additional patient identifier

Report information

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 dates for initial and final report
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 subsequent follow up report

Serious Adverse Event information

Adverse Event term:	the most accurate 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. If no diagnosis is available (yet), please provide the most relevant sign or symptom (for example "fever" or "dyspnea"), If in this case a diagnosis is available at a later date, adjust the adverse event term accordingly. If the SAE is a complex case with multiple <u>related</u> Adverse Events or symptoms occurring simultaneously, please report the most relevant AE term (as assessed by the investigator, e.g. the AE term documented in medical records as the primary reason for hospital admission). The other related AEs or symptoms should be reported in the *SAE description and comments* as concomitant AEs and please indicate that these AEs are

related to the SAE. Please report all other Adverse Events that occur at the same time and are all serious but unrelated to one another as separate SAEs.

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 met the criteria for being an SAE, this can be the same date as *Date onset AE* or later;

Reason AE is Serious: if the AE meets more than one criterion, please choose the most relevant.

Severity of AE: the highest CTCAE grade that was observed during the course of the Adverse Event; for AEs that increase in severity after the initial SAE report was sent, this item will have to be updated in the follow up or final report.

SAE description and comments

Use this box to describe the course of events from onset AE until end of the SAE. Please include dates and results of any relevant tests or procedures that were used to diagnose the SAE and actions taken to treat the SAE. For a final report also describe outcome of adverse events and all relevant test results. Please also include concomitant AEs and symptoms if applicable (see *Adverse Event term instructions).*

Outcome of the SAE

Outcome of SAE:

- resolved — the Adverse Event is no longer present
- 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
- ongoing closed (because stable situation reached) — the Adverse Event is still ongoing but no longer a Serious Adverse Event.- For example, patient was hospitalized for liver insufficiency. The liver insufficiency is still present but the liver functions have improved and patient no longer needs to be hospitalized.

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 (only in case of outcome "resolved " or "ongoing closed")

If patient died: fill out these items if “death” was 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 could be a separate SAE and may have to be reported as such. Please refer to the trial protocol.

Action taken regarding the SAE: action taken regarding the trial medication/procedure as a consequence of the Adverse Event. Please use “drug withdrawn (temporarily or permanently)” if the treatment was stopped before completion of the protocol phase during which the SAE occurred. “Not applicable” can be used in in case of death of the patient or if the treatment had been completed prior to the onset of the event (e.g. surgery).