



INSTRUCTIONS FOR REPORTING SERIOUS ADVERSE EVENTS

Form # 13B

Important: Serious Adverse Event Reports are to be reported to the DCC within 24 hours of the PCC becoming aware of the event. A paper copy of Form 13 is to be completed and signed by the investigator prior to submitting the final form to the DCC. The investigator is to determine items #7, 8, 9, 10 and 14 in section I; and items #20 and 21 in section II if applicable. For more details, refer to SAE Definitions and Reporting Guidelines outlined in section 13.7 of the Manual of Procedures (MOP).

Reporting SAEs (Temporary Method): Form 13 is to be completed and signed by the investigator. Next, fax the report with a coversheet to the DCC (fax: 412-647-0632). Next, create a Request Tracker ticket within the data queue and include "SAE" and the participant's ID in the subject line. The RT ticket will be used to track correspondences regarding the report. If necessary, report the event by phone.

A. THE ID BOX: ALL PAGES

Participant ID:

Enter the HALT-PKD Participant ID Code. Never report any personally identifying information.

Initial/Follow-up Report:

Check the appropriate blank for initial or follow-up report. Initial reports must be as complete and accurate as possible at the time of reporting. Number follow-up reports sequentially, beginning with one. For tracking, initial reports will be identified by participant, event, and onset date (date of the event). Follow-up reports will be linked to initial reports using these three identifiers. Resolved events are considered complete if all required and available information has been reported.

Date of This Report:

Enter the current date on which the report is being submitted to the DCC, regardless of whether it is an initial or follow-up report. Note that the onset date (#2 below) is static and is linked to the event being reported. If the date of the event is erroneously entered and must be corrected, the report may be tracked by participant/event, and if necessary, by date of original report.

Visit Code (optional):

Enter the current or subsequent study visit code. All adverse events (whether serious or non-serious) occurring between planned study visits are considered to occur within the "AE visit range" for the *subsequent* study visit (refer to the Manual of Procedures for definitions of study visits).

Note: Any signs, symptoms or non-serious AEs entered in text fields of SAE reports are also to be entered on Symptoms Checklist Form 5 for the subsequent visit. Any ongoing drug therapies used to treat reported events (entered in text fields 15 or 25) are also to be entered on Concomitant Medication Form 6 for subsequent visit.

B. SERIOUS ADVERSE EVENT: SECTION I

1. Serious Adverse Event Code, Term, and Severity Grade:

The investigator is to determine the appropriate term to describe the event and its severity (at its worst). Event terms/codes/severities can be found at <http://safetyprofiler-ctep.nci.nih.gov/CTC/CTC.aspx>. The study uses the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) and associated severity codes. CTCAE terms are mapped to MedDra codes.

Note: Exact terms for events may not always be available within the required reporting period. Investigators should make a best guess as to the appropriate term and later modify the report if necessary. If uncertain, investigators should err on the side of caution.



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2. Onset Date and Time:

Enter the date and time at which the event first began or became serious. Indicate if the participant is currently pregnant, or was at onset, and give the number of weeks. Mark "N/A" for male participants.

3. End Date and Time:

Enter the date and time at which the event ended (per investigator judgment).

4. Outcome of Event:

Indicate whether the event is ongoing or resolved at the time of report submission. Check "recovered" if the participant has returned to his/her previous health status with no sequelae. Check "sequelae" if the participant has a permanent change in health status subsequent to the adverse event and describe the changes in the section #15. Check "fatal" if the participant died, and provide the date and cause of death in #6, as well as whether or not an autopsy was performed.

5. Date and Time PCC Personnel Learned of the Event:

Enter the date and time study staff first learned of the event. This may be the same as the date of the event and the date of the report, but in some cases, PCCs may not learn of an event until after the fact. To avoid queries, describe reasons for delays in reporting or study staff learning of the event under #34 comments.

6. Reason the Event is Serious:

There are eight criteria by which to determine if an event is considered "serious" for the HALT study. Refer to SAE Definitions and Reporting Guidelines in the MOP section 13.7. Check all that apply.

Note: If the event results in death, obtain medical records, including death certificate, to confirm the cause of death and enter Death Notification Form 31 within two weeks.

If the event resulted in hospitalization—admission or prolongation, obtain medical records and enter Hospitalization Form 30 within two weeks.

7. Relatedness to Study Participation:

The investigator is to determine the likelihood of an event being related to study participation (i.e., caused by study procedures and/or medications). Also included in this category are events related to study-related drugs that are *not* used to control blood pressure (e.g., Kayexelate, potassium, valium). If relevant to the event, such drugs should be listed in section #32.

8. Relatedness to Blood Pressure Medication:

The investigator is to determine the likelihood of an event being related to the use of any medication used to control blood pressure (study drug), whether washout, masked (telmisartan/placebo) or open-label.

9. Relatedness to Masked Medication:

The investigator is to determine the likelihood of an event being related specifically to the use of telmisartan and placebo (this is a subcategory of #8 above).

10. Unexpected:

Once the investigator has determined whether the event is related to study medication (#8 and #9 above), he or she must then determine if the event is *unexpected*. Adverse events that are *expected* appear as risks in the informed consent. Adverse events that are unexpected are reasonably related to study medication and exceed the nature, severity or frequency of risk described in the protocol. Unexpected adverse events require expedited reporting and are to be added to the consent form, per Steering Committee discretion.

Note: If the reason an event is serious is that it "exceeds the nature, severity or frequency described in the protocol" (per Form 13, question #6, option #5), and the event is reasonably related to study medication (per Form 13, questions #8 or #9), then by definition, the event is unexpected and Form 13, question #10 must be answered "yes".



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11. Setting: Select the setting in which the event first occurred.

12. Therapy for Event:

Indicate if the participant has been given therapy for the event. Specify drug therapies and non-drug therapies *used to treat* the event in the table in #15. Provide as much detail as possible.

13. Action Taken with Masked Medication:

Indicate the action taken with masked medication due to this event (this is a subset of #28 below).

14. Relatedness to ADPKD:

The investigator is to determine if the event is related to ADPKD (to be included in the study analysis).

15. Description:

Provide a brief description (100 characters or less) of the event, including associated signs and symptoms, any unusual or concerning aspects, and results of pertinent tests and examinations confirming the event. Of particular interest are data which provide a baseline prior to use of drugs associated with the event. *In the table, include total daily dose of drug therapies, and all non-drug therapies, used to treat the event.*

C. ASSOCIATED ADVERSE EVENT(S): SECTION II

Page two is to be completed for each adverse event associated with event #1. If page two is completed, number associated adverse events beginning with #2, and number report pages according to the total number of pages in the report. In some cases, an associated adverse event will also be serious, but a separate SAE report is not necessary. In many cases, however, page two will not apply, thus "N/A" should be entered on the paper form instead of an associated adverse event number.

16. Associated Adverse Event Code, Term, and Severity Grade:

Enter the associated adverse event code, term and severity grade (at its worst) based on the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) and MedDra codes. Event terms/codes/severities can be found at <http://safetyprofiler-ctep.nci.nih.gov/CTC/CTC.aspx>. For all serious associated events, the investigator is to determine the appropriate terms and severity grades.

17. Onset Date and Time:

Enter the date and time at which an associated adverse event first began or became serious. Indicate whether the event is ongoing or resolved at the time of report submission.

18. End Date and Time:

Enter the date and time at which an associated adverse event ended (per investigator judgment).

19. Outcome of Event:

Indicate whether the associated adverse event is ongoing or resolved at the time of report submission. Check "recovered" if the participant has returned to his/her previous health status with no sequelae. Check "sequelae" if the participant has a permanent change in health status subsequent to the adverse event and describe the changes in section #25. Check "fatal" if the participant died, and provide the date and cause of death in #6, as well as whether or not an autopsy was performed.

20. Seriousness and Relatedness of Associated Adverse Event:

Indicate if the associated adverse event is serious. Refer to SAE Definitions and Reporting Guidelines in the Manual of Procedures, section 13.7. If the associated adverse event is non-serious, check "no" and skip to #21. If the associated adverse event is serious, check all reasons that apply and continue.

Note: If the event resulted in death, obtain medical records, including death certificate, to confirm the cause of death and enter Death Notification Form 31 within two weeks.

If the event resulted in hospitalization—admission or prolongation, obtain medical records and enter Hospitalization Form 30 within two weeks.



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20A. Relatedness to Study Participation:

The investigator is to determine the likelihood of the event being related to study participation (i.e., caused by study procedures and/or medications). Also included in this category are events related to study-related drugs that are *not* used to control blood pressure (e.g., Kayexelate, potassium, valium). Such drugs are to be listed in section #32.

20B. Relatedness to Blood Pressure Medication:

The investigator is to determine the likelihood of the event being related to the use of any medications used to control blood pressure (study drug), whether washout, masked (telmisartan/placebo), or open-label drug.

20C. Unexpected:

Once the investigator has determined whether the event is related to study medication (20A or 20B), he or she must then determine if the event is *unexpected*. Adverse events that are *expected* appear as risks in the informed consent. Adverse events that are *unexpected* are reasonably related to study medication and exceed the nature, severity or frequency of risk described in the protocol. Unexpected adverse events require expedited reporting and are to be added to the consent form, per Steering Committee discretion.

Note: If the reason an event is serious is that it “exceeds the nature, severity or frequency described in the protocol” (per Form 13, question #20, option #5), and the event is reasonably related to study medication (per Form 13, question #20B), then by definition, the event is *unexpected* and Form 13, question #20C must be answered “yes”.

20D. Relatedness to ADPKD:

The investigator is to determine if the event is related to ADPKD.

21. Relatedness to Masked Medication:

The investigator is to determine the likelihood of an associated event (serious or non-serious) being related to the use of masked medication (telmisartan and placebo). This is a subcategory of #20B.

22. Setting: Select the setting in which the associated adverse event first occurred.

23. Therapy for Event:

Indicate if the participant has been given therapy for the associated adverse event. Specify all drug and non-drug therapies used for the associated adverse event in the table in #25. Provide details as available.

24. Action Taken with Masked Medication:

Indicate action taken with masked medication due to the associated adverse event. This is a subset of #28.

25. Description:

Provide a brief description (100 characters or less) of the associated adverse event, including associated signs and symptoms, unusual or concerning aspects, and results of pertinent tests and examinations confirming the event. Of particular interest are data which provide a baseline prior to use of drugs associated with the event. In the table, include the total daily dose of drug therapies, and non-drug therapies, used to treat the associated adverse event.



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D. MEDICATIONS AND MEDICAL CONDITIONS: SECTION III

Page three captures information related to existing medications and medical conditions. If study drugs or concomitant medications are considered relevant to the event(s), report them here.

26. Administration of Masked Medication:

Indicate if masked medication has been properly administered (taken) up to the time of onset of the event. Enter any abnormalities in masked drug administration in #34.

27. Date of Most Recent Masked Medication:

Enter the date of the most recent dose of masked medication *prior to the event*. If unknown at the time of reporting, enter your best guess and verify it with participant and/or medical records when possible.

28. Change in Blood Pressure Medications:

Determine if there has been a change in any medication used to control blood pressure (study medication) as a result of any adverse events being reported.

29. Drug Card Number and Treatment Code:

Enter the drug card number used at event onset and indicate whether the treatment code has been broken.

30. Rechallenge of Masked Medication:

Indicate if a rechallenge of masked medication was performed (refer to items #13 and #24). If yes, indicate if the outcome was *unknown*, *positive* (event reappears after reintroduction of trial drug) or *negative* (event does not reappear after reintroduction of trial drug). If a rechallenge was performed, indicate the event number(s) for each selection and give an explanation of the outcome of the rechallenge.

31. Change in Existing Concomitant Medications:

Determine if there has been a change in any *existing* concomitant medications (relevant or non-relevant) as a result of the main event or any associated events.

Note: If *new* concomitant medications (or non-drug therapies) are added to treat the adverse event(s) being reported (see #12 and #23), enter them in #15 or #25.

32. Relevant Medications:

All existing medications (taken for BP or non-BP medications) considered relevant to the event(s) being reported are to be entered here, including masked medication (which is always considered relevant). List all relevant medications taken at the time of, or just prior to, onset of the event. Provide the medication name, formulation, strength, daily dose at onset, route of administration, start date/time and end date/time of dosing (if continuing, write "cont" in this field), and the indication for which the drug is being used. List masked medication as "telmisartan/placebo" and the indication as "hypertension".

Note: Do not list medications used to treat event(s) being reported. List these in #15 and #25.

33. Relevant Concomitant Diagnoses and Dates of Onset:

List all *relevant* medical diagnoses and dates of onset. Do not list PKD as a relevant concomitant diagnosis since it is a requirement for study participation.

34. Comments:

Provide any additional information (100 characters or less) that may be helpful to the Quality Control Committee when reviewing an SAE report. Note: Free-text data entry will not be used in data analysis.



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E. Data Entry

Using the temporary method of SAE reporting, PCC personnel should not attempt data entry of SAEs. Once the report has been faxed to the DCC, and the DCC has been properly notified of the report via Request Tracker, DCC personnel will review the faxed report and ask for clarification from the PCC as necessary. Once the report has been determined as complete and correct as possible, DCC personnel will enter the data per the final report and forward the report to Boehringer Ingelheim. The RT ticket will be updated and closed if the event has been resolved. For ongoing events, the ticket should remain open until a follow up report is submitted and the event is resolved.

F. Follow-up Reports

Initial SAE Reports are to be entered within 24 hours of the PCC becoming aware of the event. However, despite our best efforts, information available at the time of the initial report may be incomplete or incorrect. A follow-up report signed by the investigator should be faxed to the DCC in a timely fashion in order to provide more information, correct erroneous information, or report new developments, including the resolution of serious adverse events.

Choice of Methods: PCC personnel may use one of the following methods to complete the paper form:

- a) Make a photocopy of the initial report or most recent follow-up report (final version) and add follow-up data to it (use a different-colored ink, and *circle, date and initial all changes*).
- b) Print a blank copy of Form 13 and add the follow-up data to it.

Form Completion: Complete the textbox in the upper right corner of the form. Enter the participant ID, the date of the follow-up report (today's date), check "follow-up" and enter the number for the follow-up report (beginning with 1). Visit code is optional. Questions #1, 2 and 4 must be completed and should be corrected if necessary. Complete #3, if applicable, and modify #4 if necessary. Enter on the paper form *only new information to be reported*, and a description of the changes in #15, 25, or 32 if necessary.

Active Reports: SAE reports are considered active so long as a serious adverse event is ongoing. Several follow-up reports may be necessary before serious adverse events have resolved.