ADVERSE EVENTS

If a patient experiences an unusual side effect, adverse event, or a serious adverse event, complete the Adverse Event (AE) form.

An Adverse Event form should not be completed for expected symptoms of the underlying disease or common side effects, such as those listed on the Visit Evaluation form.

Adverse Event Guidelines:

At a minimum, the following criteria should be used as a guide for recording Adverse Events. These guidelines are not all inclusive and the recording of Adverse Events remains at the discretion of the investigator. A symptom or condition that is present but does not reach one of these levels may still be recorded as an adverse event.

1) A symptom or event that requires discontinuation of study medication.
2) A newly diagnosed symptom or event that requires a written prescription for treatment.
3) A newly diagnosed symptom or event that results in a referral to another provider.
4) Any grade 3 or 4 event according to the NCI Common Toxicity Criteria.

An adverse event is considered a **serious adverse event** if the event:

1. results in inpatient hospitalization or prolongs existing hospitalization
2. is life-threatening
3. results in death
4. results in significant or permanent disability
5. requires medical intervention to prevent permanent damage
6. results in a congenital anomaly or birth defect

If the patient experiences a Serious Adverse Event:

1. Clinical center personnel complete the Adverse Event form and the MEDWATCH form.

2. The completed MEDWATCH form must be faxed to the Coordinating Center at the University of Pittsburgh within 24 hours of knowledge of the event.
   Fax: (XXX) XXX-XXXX

3. The Coordinating Center will submit the MEDWATCH form to the appropriate monitor(s) and be responsible for distributing the report to the clinical center Principal Investigators, and NIH Project Officers.

4. Dr. XXXXX, holder of the IND, will be responsible for reporting to the FDA.

The Clinical Center and Coordinating Center Principal Investigators are responsible for notifying their local Institutional Review Board

ADVERSE EVENT (AE)

DATA SECTION	COMPLETION INSTRUCTIONS
GENERAL INFORMATION	The Adverse Event (AE) form is completed when the patient experiences a severe side effect, condition, or serious symptom. A form should not be completed for the presence of expected symptoms of the underlying disease or common side effects such as those captured on the Visit Evaluation form. At a minimum, adverse events that meet any of the following criteria should be reported. 1. A symptom or event that requires discontinuation of study medication. 2. A newly diagnosed symptom or event that requires a written prescription for treatment. 3. A newly diagnosed symptom or event that results in a referral to another provider. 4. Any grade 3 or 4 event according to the NCI Common Toxicity Criteria. These guidelines are not all inclusive and the recording of an adverse event remains at the discretion of the investigator. A symptom or condition that is present but does not reach one of these levels may still be recorded as an adverse event. If the adverse event is determined to be a Serious Adverse Event (SAE), complete a mandatory MEDWATCH form in addition to the Adverse Event form and return the MEDWATCH form to the Coordinating Center at the University of Pittsburgh within 24 hours of knowledge of the event. Follow the detailed instructions in the Form Completion section of this manual for AEs that evolve into SAEs. Each page of the Adverse Event form is designed to capture up to 15 events per patient. Each new onset of an adverse event should be recorded on one line of the Adverse Event form. If a patient has more than 15 adverse events, move to the next page. Each adverse event should have an onset and outcome date, regardless of the duration of the event. Do not record the same event on more than one line if the event is continuing from one evaluation to the next. Leave the Outcome Date and Outcome Status columns blank until the event either resolves or is determined to be continuing but controlled. If the Outcome Status is determined to be Continuing/controlled and then the patient has an exacerbation of that same event type, record the new onset on a new line. Only new onsets should be recorded on a new line.
PATIENT ID	Record the patient ID in the top left hand corner of the form.
PAGE	Record the page number. Each page of the Adverse Event form captures up to 15 adverse events. Begin with page 1 for each patient and continue to add pages as needed.

DATA SECTION	COMPLETION INSTRUCTIONS
	SPECIFIC INSTRUCTIONS: Date of onset: Record the date (day/month/year) that the adverse event started. If any part of the date is unknown, record "Unk" in that field and complete the remaining fields. Event type: Record the code that indicates the event type. Refer to the current code list found on the project website. Also, provide specification for the event on the back of the AE form, e.g. in the event of Death, specify the cause of death. Serious adverse event: Circle "Y" (yes) or "N" (no) to indicate if the adverse event is a serious adverse event. If yes, complete a MEDWATCH form and submit that form to the Coordinating Center within 24 hours of knowledge of the event. Severity: (1) Record the code that indicates the initial severity of the episode. (2) Record the code that indicates the "most severe" severity of the episode. 1 = mild - easily tolerated condition or symptom 2 = moderate - discomfort that interferes with usual activity 3 = severe - incapacitating or causes inability to work or undertake usual activity 4 = life threatening Relationship to study drug: Record the code that indicates the relationship of the event to the study medication. 1 = unrelated (there is no reasonable causal relationship between the study drug and the AE) 2 = unlikely 3 = possibly related 4 = probably related 5 = definitely related Effect on study drug dosing: Record the code that indicates the effect of the event on study drug dose. 1 = none 2 = reduced 3 = interrupted 4 = discontinued - drug withdrawn due to adverse event Action taken: Record the code that indicates the action taken for the adverse event. 1 = none 2 = additional therapy - patient received additional therapy (drug or non-drug) due to the adverse event. Examples of additional therapy include drugs, bedrest, physical therapy etc. Record the additional therapy within the box. 3 = hospitalization 4 = re-evaluation of laboratory results 5 = other If other, specify the action taken within the box.

DATA SECTION	COMPLETION INSTRUCTIONS
	Outcome date: Record the date (day/month/year) of the outcome of the adverse event. If the adverse event is continuing but not controlled this column should be left blank until the event is resolved or continuing and controlled. Some events may continue through the end of the study period before being resolved or determined to be continuing but controlled. Outcome status: For each adverse event, record the code that indicates the outcome status of the event. If the adverse event is continuing but not controlled record as 'continuing'. When the event is either 'resolved' or 'controlled', update both the Outcome Date and Outcome Status on the form and in the database. If the adverse event evolves into a SAE, close out the adverse event by recording complete information for the AE until the time that it was determined to be a SAE. Record 'evolved into SAE' as the Outcome Status, and record the date that the AE was determined to be a SAE as the Outcome Date. Complete a new line for the SAE. The date of onset is the date that the AE was determined to be a SAE. Record all other information on that line pertaining to the SAE. 1 = Resolved - patient returned to previous health status with no subsequent problems 2 = Continuing - patient has not yet returned to previous health status and continues to be followed for the AE 3 = Controlled - event is present but is controlled 4 = Evolved into SAE - a continuing adverse event that developed into a serious adverse event Events that are coded as Continuing will be reviewed periodically throughout the course of the study to determine whether they are Resolved or Controlled.