Protocol #: 272MS401

- Clinical Trial Serious Adverse Event (SAE) Form (RD-T-144)
- Clinical Trial Serious Adverse Event (SAE) Follow-Up Form (RD-T-145)

Use this form to report pregnancy-related SAEs only, per protocol. If the subject is enrolled in another Biogen Vumerity (BIIB098) Clinical Trial, instruct the Health Care Provider (HCP) to report non-pregnancy related SAE under that study. If the subject is not enrolled in another Biogen Vumerity (BIIB098) study, instruct the HCP to report non-pregnancy related SAEs via post market channels.

GENERAL INSTRUCTIONS FOR COMPLETING SAE FORMS

- Write legibly using a black or blue indelible ink pen.
- Provide follow-up information on the Clinical Trial Serious Adverse Event (SAE) Follow-up Form. Do not modify previously submitted Clinical Trial Serious Adverse Event (SAE) Form with follow-up data.
- If a correction is required, draw a single line through the error, so that it remains legible, write in the correct data, then initial and date the changes (e.g., ~~placebo~~ placebo EAL 01/JAN/2022).
- Use the date format of DD/MMM/YYYY (e.g., 12/JAN/2022). Partial dates are acceptable by entering a hyphen for unknown data (e.g., -/-/2022).
- Use the appropriate medical terminology; be concise.
- Remember to redact the subject's identifying information (e.g. name, initials, day/month of birth, hospital number etc.) on all source documents.
- Be sure to write the subject ID number on each page of all forms and source documents.

COORDINATING CENTER RESPONSIBILITIES

- Complete and sign the Serious Adverse Event (SAE) Form(s).
- Fax or email the SAE Form to IQVIA Lifecycle Safety **within 24 hours** of knowledge of event.
- Do not wait for the complete information before faxing or emailing the form.
- On the **Follow-Up SAE Form,** report any changes regarding the SAE, subject condition, or new information, as it becomes available.
- Follow up with the reporting HCP to provide additional information and documents needed to support the SAE's assessment **as requested** (e.g., hospital discharge summary, pathology report, autopsy results, etc.).
- Keep the original SAE Form(s) in subject's CRF binder or Site Regulatory File.

Instructions for Clinical Trial Serious Adverse Event (SAE) Form (RD-T-144)

Section A: DEMOGRAPHICS

Subject ID #: Enter the subject ID
Year of Birth: Provide the subject's year of birth (YYYY).
Gender: Pre-populated.
Ht: Enter the height and check the appropriate unit of measure - centimeters or inches.
Wt: Enter the weight and check the appropriate unit of measure - kilograms or pounds.
Is SAE related to pregnancy: Check appropriate box. If the answer is no, instruct the reporting HCP to either report via other Biogen Vumerity (BIIB098) Clinical Trial or via post market channels as appropriate.
Current enrollment in another Biogen Vumerity (BIIB098) Clinical Trial: Check the appropriate box and provide information as applicable.

Section B: EVENT AND CRITERIA FOR SERIOUS CLASSIFICATION

SAE Term: Provide the medical diagnosis. Do not provide the symptoms or name of surgical or interventional procedures unless the diagnosis is unknown or not available.

Severity: Check only one level of severity, using the protocol definitions.
Outcome at time of this SAE report: Check one. If resolved / recovered or recovered with sequelae, enter the date the event resolved. This is the date the HCP considered the SAE to be resolved, or the date the event became stable. Check only one box to record the event outcome. If the event is recovered with sequelae, detail the sequelae in the Description of Serious Adverse Event section.
Date event became serious: Enter the date the event met the criteria for serious classification (e.g., Subject experienced mild chest pain on 24/JAN/2022 and was hospitalized the following day, 25/JAN/2022, after an EKG revealed the subject suffered an acute MI. The date the event became serious is the day of hospitalization, not the date the symptoms first started).

A Serious Adverse Event (SAE) is defined as any adverse drug experience, occurring at any dose, resulting in any **one or more** of the following categories:

- **Death:** Enter the date of death and indicate if an autopsy was performed by checking the appropriate box. (Provide autopsy report if available.)
- **Initial / Prolonged Hospitalization:** Requires hospitalization or prolongs the existing hospitalization. [NOTE: Hospitalization for elective medical/surgical procedures, scheduled treatments or routine check-ups **planned prior to enrollment** may not be considered SAEs. See the protocol for specific information.] Enter the admission and discharge date for the hospitalization if available.
- **Life-threatening:** In the view of the Investigator, this event places the subject at immediate risk of death. This does not include an event that if it had occurred in a more severe form may have caused death.
- **Congenital Anomaly / Birth Defect:** That is diagnosed in a child of a subject who participated in this study.
- **Persistent or Significant Disability:** A substantial disruption of a person's ability to conduct normal life functions.
- **Medically Significant:** Medically important events, which in the opinion of the Investigator, may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in the definitions above (e.g., allergic bronchospasm requiring intensive treatment in an emergency room, or laboratory results outside the protocol defined ranges).

Dechallenge / Rechallenge: If the study drug was dechallenged or rechallenged, indicate the outcome by checking the correct box.

- Dechallenge is the clinical decision to withdraw or discontinue a drug to monitor the effect on an adverse event. A dechallenge is positive when, after removal of the drug, the adverse event subsides or disappears. A dechallenge is negative when the event persists even after removal of the drug.
- Rechallenge is the point at which a drug is given again to a patient after its previous withdrawal. A positive rechallenge is when the AE reappears once the treatment is restarted. A negative rechallenge is when the adverse effect does not reoccur after the drug has been reintroduced.

Section C: STUDY DRUG

Study drug name: Pre-populated.
Dose / Route / Frequency: Enter the dose, route, and frequency of the study drug administration (e.g., 80 mg, Orally, QW).
Date of first treatment: Enter the date of the initial dose of study drug.
Date of most recent treatment prior to the event: Enter the date of the last dose of the study drug prior to the SAE onset date.
Total number of doses prior to the event: Provide the total number of doses of study drug prior to the SAE onset date.
Action Taken with Study Drug: Indicate the action taken with the study drug in response to this event**:** Select only one option.

- No action taken
- SAE occurred prior to first dose
- SAE occurred after final dose, per protocol

- Temporarily discontinued
- Permanently discontinued: Record date of final dose

RELATIONSHIP TO STUDY DRUG AS PROVIDED BY HEALTH CARE PROVIDER (HCP): Select only one option. Descriptions of each option are as follows:

- **Not related**
  An adverse event will be considered "not related" to the use of the investigational drug if there is not a possibility that the event has been caused by the product under investigation. Factors pointing toward this assessment include but are not limited to: The lack of reasonable temporal relationship between administration of the drug and the event, the presence of a biologically implausible relationship between the product and the adverse event (e.g., the event occurred before administration of drug), or the presence of a more likely alternative explanation for the adverse event.
- **Related**
  An adverse event will be considered "related" to the use of the investigational drug if there is a possibility that the event may have been caused by the product under investigation. Factors that point toward this assessment include but are not limited to: A positive rechallenge, a reasonable temporal sequence between administration of the drug and the event, a known response pattern of the suspected drug, improvement following discontinuation or dose reduction, a biologically plausible relationship between the drug and the adverse event, or a lack of an alternative explanation for the adverse event.

State rationale for relationship to study drug: Briefly describe the HCP's reasoning for the assessment.

If the HCP believes that the adverse event is not related to study drug but is potentially related to the conditions of the study (such as withdrawal of previous therapy or a complication of a study procedure), the relationship must be specified in the Description of Serious Adverse Event section.

Section D: MEDICAL HISTORY

Date of diagnosis of Multiple Sclerosis: Provide date of diagnosis.
Include all relevant medical history and indicate if the condition is past or present. Enter the start and stop dates. If the day and/or month are not known, enter a hyphen for the day and month (e.g., -/-/2021). If there is no stop date for a diagnosis, leave the column blank. Leave blank if the condition is ongoing. If unknown, enter "UNK."

Section E: CONCOMITANT MEDICATION

Enter medications that are ongoing or completed within one week prior to the event onset. **DO NOT INCLUDE MEDICATIONS used to treat the event in this section**.

- Provide the indication for the drug / therapy.
- Provide the dose, route, frequency, and indication, if applicable.
- **Start Date:** If the day and/or month are not known, enter a hyphen for the day and/or month (e.g., -/-/2021).
- **Stop Date:** If the day and/or month are not known, enter a hyphen for the day and/or month (e.g., -/-/2021).
  - If there is no stop date for medication, leave the column blank.
  - If the medication is ongoing, leave the column blank.

Section F: SAE TREATMENTS OR MEDICATIONS

Include all pharmaceutical and non-pharmaceutical treatments that were used to treat this event.

- Provide date treatment or medication was provided.
- Provide name of treatment or medication.
- Provide indication or medication used for treatment.

Section G: TEST(S) PERFORMED TO EVALUATE SERIOUS ADVERSE EVENT

- Provide date, name of test, test result, and laboratory normal ranges or units, if available (e.g., BUN = 8 mg/dL; Normal = 10-20 mg/dL).
- Provide copies of relevant reports (e.g., CBC results with laboratory normals, chest x-ray report, cytology report, MRI reports, etc.). Send relevant reports as supplemental documents. The relevant reports do not need to be translated into English prior to sending.

Section H: DESCRIPTION OF SERIOUS ADVERSE EVENT

Provide a chronological description, in narrative form, of the SAE. Include relevant medical history, concurrent illnesses, medical status prior to the event, diagnosis, clinical course, treatment and outcome, if available. When appropriate, attach copies of supporting labs and tests. Comment on the subject's current dosing status (i.e., enrolled and dosing, pre-dosing, withdrawn previously, discontinued due to the event but will resume dosing, etc.). If available, forward copies of the admission and discharge summaries.

Section I: HEALTH CARE PROVIDER (HCP) INFORMATION

Provide the name, title, institution, address, country, phone #, fax #, relationship to patient and the HCP best qualified to make a causality assessment for the reported event (e.g., obstetrician, neurologist, pediatrician, etc.). The coordinating center will make the determination as to which HCP is best qualified to provide a causality assessment for the event.

Section J: SIGNATURE AND COORDINATING CENTER REPRESENTATIVE INFORMATION

- The Coordination Center Representative **MUST SIGN** to acknowledge completeness and accuracy of the SAE Form.
- Print the full name and title of the Coordinating Center Representative, the date signed, the name, institution, address, country, phone, and fax number.

Instructions for Clinical Trial Serious Adverse Event (SAE) Follow-Up Form (RD-T-145)

FOLLOW-UP REQUESTS

Queries will be generated to request data for missing or incomplete fields. Source documents may also be requested. Only request from the HCP source documents as requested. Provide follow-up to queries on the Clinical Trial Serious Adverse Event (SAE) Follow-up Form.

Clinical Trial Serious Adverse Event (SAE) Follow-up Form (RD-T-145)

- Use this separate form each time new or additional information is available, corrections concerning an existing SAE are reported or when providing answers to queries.
- **Subject ID #:** Enter the subject ID.
- Provide the subject's year of birth (YYYY).
- **SAE Term:** Write the current event term for the SAE. Reassess causality if the SAE term differs from what was initially reported.
- **SAE Start Date:** Record the event start date.
- **Outcome at time of the SAE follow-up report:** Check one outcome. If fatal, provide the date of death; if recovered / resolved or recovered with sequelae, provide the date the even was resolved. If the event is recovered with sequelae, detail the sequelae in the Description of Follow-Up Information section.
- If the SAE term has changed, provide the **new causality assessment** by checking the appropriate "Not related" or "Related" box.
- Provide description of follow-up information.
- HCP: Provide the name, title, institution, address, country, phone #, fax #, relationship to patient and the HCP best qualified to make a causality assessment for the reported event (e.g., obstetrician, neurologist, pediatrician, etc.). The coordinating center will make the determination as to which HCP is best qualified to provide a causality assessment for the event.
- The Coordination Center Representative **MUST SIGN** to acknowledge completeness and accuracy of the SAE Form.
- Print the full name and title of the Coordinating Center Representative, sign, the date signed, the name, institution, address, country, phone, and fax number.