BLA 125104/S-971

GENERAL ADVICE

Biogen, Inc.
Attention: Priya Singhal
Senior Vice President, Global Safety and Regulatory Sciences
225 Binney Street
Cambridge, MA 02142

Dear Ms. Singhal:

Please refer to your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for Tysabri (natalizumab).

We also refer to the supplement approval letter issued on October 5, 2020.

The referenced approval letter included the following errors in the REMS materials:

(1) Omission of the Change Prescriber Authorization Form

The REMS materials that were omitted are appended to this letter.

If you have any questions, call Kristen Haslam, Regulatory Project Manager, at 240-402-4246.

Sincerely,

{See appended electronic signature page}

Alice T.D. Hughes, MD
Deputy Director for Safety
Division of Neurology 2
Office of Neuroscience
Center for Drug Evaluation and Research

TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Biogen
Fax: 1-800-840-1278
Phone: 1-800-456-2255

Change Prescriber Authorization

By Facsimile

PRESCRIBER AUTHORIZATION REQUESTED

Date:	<Current_Date>	Patient Enrollment Number:	<Alt_ID>
New Prescriber:	<Phys_First_Name> <Phys_Last_Name>	Patient Name:	<Pat_First_Name> <Pat_Last_Name>
Address:	<MD_Address>	Patient DOB:	<Pat_DOB>
	<MD_City>, <MD_State> <MD_Zip>	Patient Enrollment Period:	Pat_Auth_Begin> through <Pat_Auth_End>
Phone:	<MD_Phone>	Infusion Site:	
Fax:	<MD_Fax>	Infusion Site Address:	
Prescriber DEA:		Prescriber State License Number:	

Our records indicate that <Pat_First_Name> <Pat_Last_Name> will continue his/her TYSABRI (natalizumab) therapy under your care. If you agree to accept this patient, please sign this form and fax it to Biogen at 1-800-840-1278.

If you do not accept this patient or have questions about the TOUCH® Prescribing Program Requirements, please call the TOUCH Prescribing Program at 1-800-456-2255. We are available Monday through Friday.

I accept <Pat_First_Name> <Pat_Last_Name> under my care for TYSABRI (natalizumab) treatment.

Prescription for TYSABRI

Dose: TYSABRI® (natalizumab) 300 mg Dispense: 1 vial Refills: 12 Directions: IV infusion per Prescribing Information every 4 weeks

I authorize Biogen as my designated agent and on behalf of my patient to (1) use the information on this form to continue the enrollment of the above-named patient in the TOUCH Prescribing Program, (2) forward the prescription by fax or by another mode of delivery to a pharmacy, if applicable, and (3) coordinate delivery of TYSABRI on behalf of the above named patient.

_____ _____

Prescriber Signature **Date**

FAX this signed form to 1-800-840-1278

For full Prescribing Information including Boxed Warning, please see www.TYSABRI.com

Biogen

TYSABRI® (natalizumab)

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ALICE HUGHES
10/08/2020 01:06:55 PM

BLA 125104/S-971

SUPPLEMENT APPROVAL

Biogen, Inc.
Attention: Priya Singhal
Senior Vice President, Global Safety and Regulatory Sciences
225 Binney Street
Cambridge, MA 02142

Dear Ms. Singhal:

Please refer to your supplemental biologics license application (sBLA), dated and received August 6, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for Tysabri (natalizumab).

This Changes Being Effected supplemental biologics application provides for proposed modifications to the approved Tysabri risk evaluation and mitigation strategy (REMS).

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Tysabri (natalizumab). was originally approved on October 7, 2011, and the most recent REMS modification was approved on June 17, 2020. The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of removal of the patient social security number field from the Patient/Prescriber Enrollment Forms.

Your proposed modified REMS, submitted on August 6, 2020, amended and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on October 7, 2011.

There are no changes to the REMS assessment plan described in our June 1, 2020, letter.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.

e) If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use: Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including:* Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications,* provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

BLA 125104 REMS ASSESSMENT METHODOLOGY
(insert concise description of content in bold capital letters, e.g., ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT PLAN, DRUG USE STUDY)

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

BLA 125104 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR BLA 125104/ S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 125104/ S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 125104/ S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 125104/ S-000
REMS ASSESSMENT
PROPOSED MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR BLA 125104

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word format is preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

FDA can accept the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, as soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in SPL format using the FDA automated drug registration and listing system (eLIST).

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Kristen Haslam, Regulatory Project Manager, at 240-402-4246.

Sincerely,

{See appended electronic signature page}

Alice T.D. Hughes, MD
Deputy Director for Safety
Division of Neurology 2
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE:
- REMS

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ALICE HUGHES
10/05/2020 09:49:20 AM