DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 761029/S-002 and S-007

SUPPLEMENT APPROVAL
REMS MODIFICATION NOTIFICATION

Biogen Inc.
Attention: Trevor Mill
Senior Vice President, Regulatory Affairs
14 Cambridge Center
Cambridge, MA 02142

Dear Mr. Mill:

Please refer to your Supplemental Biologics License Applications (sBLAs), submitted under section 351(a) of the Public Health Service Act for Zinbryta (daclizumab) injection 150 mg/ml:

Application	Submitted on:	Received on:
BLA 761029/S-002	February 28, 2017	February 28, 2017
BLA 761029/S-007	July 7, 2017	July 7, 2017

These Prior Approval supplemental biologics applications provide for revisions to the prescribing information related to the risk of hepatic injury, infections, and immune-mediated reactions, including the addition of a new subsection of Section 5.2 (Warnings and Precautions; Immune-Mediated Disorders) describing the risk for autoimmune hemolytic anemia.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the prescribing information, Medication Guide, and Instructions for Use) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As"

at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in these supplemental applications.

All promotional materials for your drug product that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in these supplements, including any new safety information [21 CFR 601.12(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4) to the address above, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENT

The REMS for Zinbryta (daclizumab) was originally approved on May 27, 2016. The REMS consists of a communication plan, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

We also refer to your proposed REMS modification submitted on May 5, 2017, and to the labeling changes approved in this letter that pertain to the risks of hepatic injury and immune-mediated reactions.

In accordance with section 505-1(g)(4)(B) of the Federal Food, Drug, and Cosmetic Act (FDCA), we have determined that your approved REMS for Zinbryta (daclizumab) must be modified to ensure that the benefits of the drug outweigh its risks. This determination is based on the need to conform the approved REMS to the safety labeling changes approved in this letter. Your proposed modified REMS must include changes to the REMS document and REMS materials to conform to these labeling changes.

The timetable for submission of assessments of the proposed modified REMS may remain the same as that approved on May 27, 2016.

The proposed REMS modification may be submitted as an amendment to the REMS modification supplement currently under review, supplement 5. Alternatively, the proposed REMS modification may be submitted as a new and separate supplement to your application. The submission should include a new proposed REMS document and REMS materials, as appropriate, that show the complete previously approved REMS with all proposed modifications

highlighted. If you submit a separate supplement, the new submission, although subject to review under 505-1(h)(2)(A)(iii), should also reflect the REMS changes proposed in your May 5, 2017, submission (which would continue to be separately reviewed).

In addition, the submission should also include an update to the REMS supporting document that includes a description of all proposed modifications and their potential impact on other REMS elements. Revisions to the REMS supporting document should be submitted with all changes marked and highlighted.

Because we have determined that a modified REMS as described above is necessary to ensure the benefits of Zinbryta (daclizumab) outweigh the risks, you must submit your proposed REMS modification within 30 days of the date of this letter.

Because FDA is requiring the REMS modifications in accordance with section 505-1(g)(4)(B), you are not required to submit an adequate rationale to support the proposed modifications, as long as the proposals are consistent with the modifications described in this letter. If the proposed REMS modification supplement includes changes that differ from the modifications described in this letter, an adequate rationale is required for those additional proposed changes in accordance with section 505-1(g)(4)(A).

If you submit the proposed modified REMS as an amendment to your application, prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

BLA 761029/S-05
PROPOSED REMS MODIFICATION-AMENDMENT

If you submit the proposed modified REMS as a new, separate supplement, submit it as a Prior Approval supplement (PAS) to your BLA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

NEW SUPPLEMENT FOR BLA 761029/S-xxx
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABEL CHANGES SUBMITTED IN SUPPLEMENTS 2 and 7

Prominently identify subsequent submissions related to the proposed REMS modification with the following wording in bold capital letters at the top of the first page of the submission:

BLA 761029/S-xxx
PROPOSED REMS MODIFICATION-AMENDMENT

To facilitate review of your submission, we request that you submit the amendment to your proposed modified REMS in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

In addition to submitting the proposed modified REMS as described above, you can also submit the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, include the SPL file with your proposed REMS modification submission.

For more information on submitting REMS in SPL format, please email REMS_Website@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, email Laurie Kelley, Regulatory Project Manager, at laurie.kelley@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Alice Hughes, M.D.
Deputy Director for Safety
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ALICE HUGHES
08/28/2017