BLA 125499/S-21

SUPPLEMENT APPROVAL

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

Dear Dr. Singhal:

Please refer to your supplemental biologics license application (sBLA), dated and received March 30, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for Plegridy (pegylated interferon beta-1a) injection.

This Prior Approval sBLA provides for an intramuscular route of administration of Plegridy. Additionally, in accordance with the Release from Postmarketing Requirement (PMR) letter dated January 26, 2021, where you were informed of your release from PMR 2760-2, all references to a pregnancy registry have been removed from labeling.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

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 FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide) 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 *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible via publicly available labeling repositories.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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 Microsoft Word format that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on November 6, 2020, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 125499/S-21**." Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages less than 10 years because necessary studies are impossible or highly impracticable. This is because the number of patients with multiple sclerosis in this age group is very small.

We are deferring submission of your pediatric studies for ages 10 to less than 18 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

4000-1 Extrapolation of the findings from studies conducted under PMR 2760-1 (a randomized, controlled, parallel group superiority trial in pediatric patients ages 10 through 17 years to evaluate the safety and efficacy of Plegridy [peginterferon beta-1a administered subcutaneously] compared to an appropriate control for the treatment of relapsing forms of multiple sclerosis) to the intramuscular (IM) route of administration of Plegridy. If the results of the studies 105MS306 or 800MS301 (the studies being conducted under PMR 2760-1) do not support this extrapolation, separate studies to evaluate the efficacy, safety, and pharmacokinetics (PK) of IM Plegridy should be conducted.

Study Completion: 12/2023
Final Report Submission: 10/2024

The reports of this required pediatric postmarketing study must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from this study. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

2760-3 Re-evaluate the acceptance criteria release and stability specifications for Plegridy (peginterferon beta-1a) drug substance (DS) and reevaluate Plegridy (peginterferon beta-1a) drug product (DP) release and stability specification acceptance limits for: cytopathic effect potency (CPE) assay, (b) (4), high molecular weight impurities as measured by size exclusion chromatography, and (b) (4) and purity as measured by reverse phase HPLC for drug product. Justify revised acceptance data using data collected from production scale Plegridy (peginterferon beta-1a) DS and DP manufactured using 30 distinct DS batches and knowledge about the clinical importance of product quality attributes. The re-evaluation will be submitted as a prior approval supplement after data is analyzed from the DP and DS batches or within three years, whichever is sooner.

The timetable you submitted on May 1, 2014, states that you will conduct this study according to the following schedule:

Submission due date: 09/30/2017

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

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, please contact Rania Younes, Regulatory Project Manager, via email at rania.younes@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Paul R. Lee, MD, PhD
Deputy Director
Division of Neurology 2
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

---

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/

PAUL R LEE
01/29/2021 09:40:59 AM