BLA 103471/S-5199

APPROVAL LETTER

Bayer Healthcare Pharmaceuticals Inc
Attention: Rashmi John, MD
Associate Director, Regulatory Affairs
100 Bayer Blvd
P.O. Box 915
Whippany, NJ 07891-0915

Dear Dr. John:

Please refer to your sBLA dated and received November 20, 2020, submitted under section 351(a) of the Public Health Service Act for Betaseron (interferon beta-1b) for injection.

This Prior Approval supplemental biologics application proposes to seek approval for the following changes to the BLA:

1. Change the approved long-term storage conditions for interferon beta-1b drug product (b) (4).
2. Change the approved stability protocols (b) (4) (b) (4) (b) (4) and to change the stability testing frequency from every 25 batches, to at least one batch per year.
3. Change of the corresponding labeling information to accommodate this approved change of drug product storage condition (b) (4) (b) (4) as part of a revised range that includes the historic minimum approved drug product storage condition (b) (4).

APPROVAL & LABELING

We have completed our review of this supplemental application. 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, 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.

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, 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).

We have the following labeling recommendations for your consideration.

A. General Comments

1. Your labeling includes the following.

> Manufactured for:
> Bayer HealthCare Pharmaceuticals Inc.
> Whippany, NJ 07981

According to 21 CFR 610.64 (bold emphasis added),

> The name and address of the distributor of a product may appear on the label provided that the name, address, and license number of the manufacturer also appears on the label and the name of the distributor is qualified by one of the following phrases: "**Manufactured for** _____", "Distributed by _____", "Manufactured by _____ for _____", "**Manufactured for** _____ by ____", "Distributor: _____", or "Marketed by _____". The qualifying phrases may be abbreviated.

Qualifying the name of the applicant with "Manufactured for," may suggest that Bayer HealthCare Pharmaceuticals Inc. is the name of the distributor of the drug product which is not the case. According to 21 CFR 600.3(t), the manufacturer is the Applicant/licensee. Please revise to clearly indicate the manufacturer of your drug product.

2. The appropriate package-type term for this product is "single-dose" rather than "single-use." Please refer to "Selection of the Appropriate Package Type Terms

and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use Guidance for Industry" and revise accordingly. The guidance can be found at https://www.fda.gov/media/117883/download.

3. Consider revising the country of origin to read "Product of Germany."

B. Prescribing Information

Please consider revising the first sentence of the first paragraph in the DESCRIPTION section to read "Interferon beta-1b is a purified, sterile, lyophilized protein product produced by recombinant DNA techniques."

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to carton and container labeling submitted on November 20, 2020, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels 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 "**Product Correspondence – Final Printed Carton and Container Labeling for approved BLA 103471/S-5199.**" Approval of this submission by FDA is not required before the labeling is used.

This information will be included in your biologics license application file.

If you have any questions, call Teshara G. Bouie, Quality Assessment Lead (Acting), at (301) 796 - 1649.

Sincerely,

{See appended electronic signature page}

Gibbes Johnson, Ph.D.
Director
Division of Biotechnology Review and Research IV
Office of Biotechnology Products
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

[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.

Enclosures:
Content of Labeling
Carton and Container Labeling

Gibbes Johnson

Digitally signed by Gibbes Johnson
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