DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 103964/S-5270

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Hoffmann-La Roche, Incorporated
c/o Genentech, Incorporated
Attention: Peggy Omoruan
Program Manager, Regulatory Affairs
1 DNA Way
South San Francisco, CA 94080-4990

Dear Ms. Omoruan:

Please refer to your Supplemental Biologics License Application (sBLA), dated and received December 15, 2016, and your amendments, submitted under section 351(a) of the Public Health Service Act for PEGAYS® (peginterferon alfa-2a) injection for subcutaneous use, 180 mcg/mL Vial, 180 mcg/0.5 mL Prefilled Syringe, 135 mcg/0.5 mL and180 mcg/0.5 mL Autoinjector.

We also refer to our approval letter dated October 13, 2017, which contained the following errors:

- Dates not updated under Recent Major Changes; and
- Medication Guide not included.

This replacement approval letter incorporates the correction of the errors. The effective approval date will remain October 13, 2017, the date of the original approval letter.

This Prior Approval supplemental biologics application provides data and labeling revisions from clinical study YV25718 for the treatment of non-cirrhotic pediatric patients 3 years of age and older with HBeAg-positive Chronic Hepatitis B virus infection and evidence of viral replication and elevations in serum alanine aminotransferase.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is 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 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 titled "SPL Standard for Content of Labeling Technical Qs and As" athttp://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 this supplemental application.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for children less than 3 years of age because necessary studies are impossible or highly impracticable as the number of pediatric patients is too small and there is evidence strongly suggesting that the drug product would be unsafe in this age group.

We note that you have fulfilled the pediatric study requirement for ages 3 to less than 18 years for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated December 15, 2016, containing the final report for the following postmarketing requirement listed in the May 13, 2005 approval letter for BLA 103964/S-5037:

2322-1 To assess the safety and efficacy of Peginterferon alfa-2a versus a no-treatment control in 110 pediatric HBeAg positive patients chronically infected with the hepatitis B virus, who have compensated liver disease.

We have reviewed your submission and conclude that the above requirement is fulfilled.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our May 13, 2005 letter.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

3280-1 Submit the final clinical study report including the data from the ongoing extended long-term follow-up phase for the Study YV25718 entitled, "A phase IIIb parallel-group, open-label study of pegylated interferon alfa-2a (PEG-IFN), monotherapy compared to untreated control in children with HBeAg positive chronic hepatitis B in the immune active phase." The final report should include data on growth parameters to assess long-term impact on growth and on other safety parameters collected as specified in the final study protocol. In addition, available data on hepatitis B serologic markers should be included to assess durability of response.

The timetable you submitted on September 21, 2017, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	06/2014
Trial Completion:	12/2021
Final Report Submission:	12/2022

We note, you submitted the clinical protocol to your IND 10144 for this product. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **"Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."**

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the prescribing information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research

Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments 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).

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 http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, 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).

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 Victoria Tyson, Regulatory Project Manager, at (301) 796-0827.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
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/

JEFFREY S MURRAY
10/13/2017