DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 103411/S-5196

SUPPLEMENT APPROVAL

Baxalta US Inc.
Attention: Kathleen Croal
Associate Director, Regulatory Affairs
650 East Kendall Street
Cambridge, MA 02142

Dear Ms. Croal:

Please refer to your Supplemental Biologics License Application (sBLA), dated March 2, 2018, received March 5, 2018, and your amendments, submitted under section 351(a) of the Public Health Service Act for Oncaspar® (pegaspargase) injection, 3,750 IU/5 mL (750 IU/mL).

This Prior Approval supplemental biologics application provides for revisions to the labeling for Oncaspar that include clarification of the age groups in the intended population for the indications in Section 1; instructions for a new dose for adults, a new dose modification table, and updates to the Preparation and Administration subsection of Section 2; updates to the warnings for hypersensitivity, pancreatitis, hemorrhage and hepatotoxicity in Section 5; deletion of the Study 2 safety summary, addition of detailed safety data from Study DFCI 11-001 Oncaspar arm, and addition of postmarketing safety data in Section 6; deletion of Section 7; revisions to comply with PLLR and updates to the pediatric use subsection of Section 8; clarifications in Sections 11, 12 and 16; additional PK information from Study AALL07P4 in Section 12; updates to the PK results for CCG-1962 in Section 14, and updates to the counseling information in Section 17.

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 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 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).

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.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments with the timetable you submitted on January 3, 2019, states that you will conduct this study according to the following schedules:

PMC 3563-1 Develop and validate screening and confirmatory assays for the evaluation of anti-pegaspargase antibodies. Develop an assay to determine whether any anti-pegaspargase antibodies are anti-PEG. Submit the final reports in accordance with 21 CFR 601.12.

Final Report Submission: 01/2019

PMC 3563-2 Reanalyze the remaining immunogenicity samples from study DFCI 11-001 to determine the incidence of anti-pegaspargase and anti-PEG antibodies using the ADA validated assays from PMC 1. For any newly confirmed positive samples, evaluate the neutralizing capacity of the anti-pegaspargase antibodies with the validated integrated binding ADA/serum asparaginase activity assays. Submit the final study report in accordance with 21 CFR 601.12.

Final Report Submission: 12/2019

Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies 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.

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 Kimberly Scott, Regulatory Project Manager, at (240) 402-4560.

Sincerely,

{See appended electronic signature page}

Albert Deisseroth, MD, PhD
Supervisory Associate Division Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling
Prescribing Information

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/

ALBERT B DEISSEROTH
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