

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761125Orig1s000

Trade Name: BEOVU (brolucizumab-dbl) injection for intravitreal injection.

Generic or Proper Name: brolucizumab-dbl

Sponsor: Novartis Pharmaceuticals Corporation

Approval Date: October 7, 2019

Indication: indicated for the treatment of Neovascular (Wet) Age-Related Macular Degeneration (AMD)

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APPROVAL LETTER



BLA 761125

BLA APPROVAL

Novartis Pharmaceuticals Corporation
Attention: Franklin Akomeah, PhD
Global Regulatory Director
4800 Overton Plaza
Suite 300
Fort Worth, TX 76109

Dear Dr. Akomeah:

Please refer to your biologics license application (BLA) dated and received February 7, 2019, and your amendments, submitted under section 351(a) of the Public Health Service Act for BEOVU (brolocizumab-dblI) injection for intravitreal injection.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 1244 to Novartis Pharmaceuticals Corporation, East Hanover, NJ under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product BEOVU (brolocizumab-dblI) injection. BEOVU is indicated for the treatment of neovascular age-related macular degeneration.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture BEOVU drug substance at (b) (4) (b) (4). The final formulated drug product will be manufactured, filled, labeled, and packaged at Novartis Pharma Stein AG, Stein, Switzerland. Secondary packaging will occur at Novartis Pharma Stein AG, Stein, Switzerland, (b) (4) (b) (4).

(b) (4) You may label your product with the proprietary name, BEOVU, and market it in a vial kit including one 6 mg/0.05 mL dosage in a 2 mL single-dose vial of BEOVU and a filter needle.

DATING PERIOD

The dating period for BEOVU shall be 18 months from the date of manufacture when stored at 5°C ± 3°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) (b) (4) months from the date of manufacture when stored at less than (b) (4) (b) (4) °C.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of BEOVU and each kit component to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of BEOVU, or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

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, which is identical to the package insert submitted on October 3, 2019.

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 Content of labeling must be identical to the enclosed labeling (Prescribing Information). 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.

CARTON AND CONTAINER LABELING

We acknowledge your September 18 and 27, and October 4, 2019, submissions containing printed carton and container labeling. Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling 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 761125.**” Approval of this submission by FDA is not required before the labeling is used.

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 at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

ADVISORY COMMITTEE

Your application for BEOVU was not referred to an FDA advisory committee because this biologic was not the first product licensed for this indication and the evaluation of the safety and efficacy data in the treatment of neovascular age-related macular degeneration did not raise significant safety or efficacy issues that were unexpected for a biologic of this class.

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 this application because neovascular age-related macular degeneration does not occur in pediatric patients.

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

We remind you of your post-marketing commitments, as agreed in the timetable submitted on August 13, 2019:

3691-1 Complete method development and implement a method (b) (4) (b) (4) for a drug substance in-process control.

Method development completed: 12/31/2019
Evidence of implementation of testing: 04/30/2020
Limit of (b) (4) test results: First Annual Report

3691-2 Complete an accelerated leachables study using the final container closure system with both brolicizumab drug product and the most appropriate representative buffer.

Final Report Submission: 09/30/2020

3691-3 Use samples from three drug substance lots manufactured using the commercial process at (b) (4) to qualify the drug substance in process and release methods for the bioburden test and drug substance in process method for the endotoxin test.

Final Report Submission: 01/31/2020

- 3691-4 Develop an endotoxin detection method capable of detecting endotoxin from the drug product.

Final report submission: 12/31/2019

Implementation of the testing method: 04/30/2020

Submit nonclinical and chemistry, manufacturing, and controls protocols and all post-marketing 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 post-marketing 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 post-marketing commitments should be prominently labeled “**Post-marketing Commitment Protocol**,” “**Post-marketing Commitment Final Report**,” or “**Post-marketing 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, Medication Guide, and Patient Package Insert (as applicable) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Patient Package Insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.³ Information and Instructions for completing the form can be found at FDA.gov.⁴ For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.⁵

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80).

³ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁵ <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at [FDA.gov](http://www.fda.gov).⁶

⁶ <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Dheera Semidey, Regulatory Project Manager, at 301-796-3009.

Sincerely,

{See appended electronic signature page}

Peter P. Stein, MD
Director
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information
 - Outer Carton (Trade)
 - Outer Carton (Sample)
 - Inner Carton (Trade)
 - Inner Carton (Sample)
 - Vial Label (Trade)
 - Vial Label (Sample)

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/

PETER P STEIN
10/07/2019 05:49:20 PM