BLA 761274

BLA APPROVAL

Biocon Biologics Inc.
Attention: Paul V. Thomas
Global Head Portfolio and Program Management
245 Main St., 2nd Floor
Cambridge, MA 02142

Dear Paul Thomas:

Please refer to your biologics license application (BLA) dated and received October 29, 2021, and your amendments, submitted under section 351(k) of the Public Health Service (PHS) Act for Yesafili (aflibercept-jbvf) injection.

We acknowledge receipt of your amendment dated November 27, 2023, which constituted a request for approval following our November 16, 2023 provisional determination letter. This BLA provides for Yesafili (aflibercept-jbvf) injection, 2 mg (0.05 mL of 40 mg/mL) for intravitreal use in a single-dose vial kit as interchangeable with US-licensed Eylea (aflibercept) injection, 2 mg (0.05 mL of 40 mg/mL) for intravitreal use in a single-dose vial kit and single-dose pre-filled syringe.

LICENSING

We have approved your BLA for Yesafili (aflibercept-jbvf) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Yesafili (aflibercept-jbvf) under your existing Department of Health and Human Services U.S. License No. 2324. Yesafili is indicated for neovascular (wet) age-related macular degeneration, macular edema following retinal vein occlusion, diabetic macular edema, and diabetic retinopathy.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture aflibercept-jbvf drug substance at (b) (4). The final formulated drug product will be manufactured and filled at (b) (4). The filled drug product will be labeled and packaged at (b) (4). You may label your product with the proprietary name, Yesafili, and market it as 2 mg (0.05 mL of 40 mg/mL solution) in a single-dose vial.

DATING PERIOD

The dating period for Yesafili shall be 36 months from the date of manufacture when stored at 2°C to 8ºC, protected from light. 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) months from the date of manufacture when stored at (b) (4).

The expiration date for the packaged product, Yesafili plus Injection Kit (30-gauge ½ inch injection needle, 18-gauge 1 ½ inch 5 mm filter needle, 1 mL syringe) shall be dependent on the shortest expiration date of any component.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Yesafili 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 Yesafili, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

FIRST INTERCHANGEABLE EXCLUSIVITY

Section 351(k)(6) of the PHS Act provides:

> The Secretary shall not make approval as an interchangeable biological product effective with respect to an application submitted under this subsection that relies on the same reference product for which a prior biological product has received a determination of interchangeability for any condition of use, until the earlier of—
>
> (A) 1 year after the first commercial marketing of the first interchangeable biosimilar biological product to be approved as interchangeable for that reference product;
>
> (B) 18 months after—
>
> > (i) a final court decision on all patents in suit in an action instituted under subsection (l)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(ii) the dismissal with or without prejudice of an action instituted under subsection (l)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(C)

(i) 42 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has been sued under subsection (l)(6) and such litigation is still ongoing within such 42-month period; or

(ii) 18 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has not been sued under subsection (l)(6).

For purposes of this paragraph, the term “final court decision” means a final decision of a court from which no appeal (other than a petition to the United States Supreme Court for a writ of certiorari) has been or can be taken and the term “first interchangeable biosimilar biological product” means any interchangeable biosimilar biological product that is approved on the first day on which such a product is approved as interchangeable with the reference product.

Yesafili (aflibercept-jbvf) injection, 2 mg (0.05 mL of 40 mg/mL) for intravitreal use is the first product relying on its reference product to receive a determination of interchangeability for any condition of use. Therefore, with this approval, this product qualifies as a first interchangeable biosimilar biological product for purposes of section 351(k)(6) of the PHS Act. The expiration date of any first interchangeable exclusivity has yet to be determined.

For each interchangeable biosimilar biological product approved by this letter, submit a general correspondence to this 351(k) BLA informing the Agency of the date of the first commercial marketing within 30 days of such date. Submit a duplicate copy of the correspondence via email to PurpleBook@fda.hhs.gov.

If applicable, please submit a general correspondence to this 351(k) BLA informing the Agency of the date of any final court decision (as defined in section 351(k)(6) of the PHS Act) on all patents in suit in any action implicating this BLA instituted under section 351(l)(6) of the PHS Act, or the date of dismissal with or without prejudice of any action implicating this BLA instituted under section 351(l)(6), within 30 days of such date or within 30 days of this approval if such date occurred prior to approval. If any action implicating this BLA instituted under section 351(l)(6) is still ongoing at the time of this approval, submit a general correspondence informing the Agency of this within 30 days of this approval. Submit a duplicate copy of the correspondence(s) via email to PurpleBook@fda.hhs.gov.

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.[1] Content of labeling must be identical to the enclosed labeling (text for the 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 (October 2009)*.[2]

The SPL will be accessible via publicly available labeling repositories.

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 *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761274**." 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

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[1] See 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.

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

We remind you of your postmarketing commitments:

4611-1 Perform a real-world shipping validation study for M710 drug product shipped from (b) (4) to (b) (4). The study will be performed using 3 representative commercial M710 drug product lots shipped under worst-case commercial shipping conditions and include the evaluation of M710 biochemical quality attributes from samples collected prior to and after shipment. The real-world shipping validation study design and results will be submitted in the final report to the BLA.

The timetable you submitted on March 6, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 4/2025

4611-2 Perform method verification studies to confirm the suitability of the USP <789> *Particulate Matter in Ophthalmic Solution* method for its intended use during M710 drug product lot release and stability testing at each commercial testing site. The method verification study results will be provided in the final study report to the BLA.

The timetable you submitted on March 6, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 4/2025

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]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

[21 CFR 314.81(b)(3)(i)]. 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

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

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

You must submit distribution reports under the distribution reporting requirements at 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

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, please contact Diana Willard, Chief Project Management Staff, at diana.willard@fda.hhs.gov or at (301) 796-0833.

Sincerely,

{See appended electronic signature page}

Charles J. Ganley, MD
Director
Office of Specialty Medicine
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
    - Prescribing Information
- Carton and Container Labeling

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/

CHARLES J GANLEY
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