BLA 761377/Original 1

BLA APPROVAL

CELLTRION, Inc.
c/o Parexel International
Attention: Ally Danta
Regulatory Affairs Consultant
541 Church at North Hills St., Suite 1000
Raleigh, NC 27609

Dear Ally Danta:

Please refer to your biologics license application (BLA) received June 29, 2023, and your amendments, submitted under section 351(k) of the Public Health Service Act for Eydenzelt (aflibercept-boav) injection.

We acknowledge receipt of your resubmission dated April 18, 2025, which constituted a complete response to our March 26, 2025, action letter.

This BLA seeks licensure of Eydenzelt (aflibercept-boav) as follows:

- Eydenzelt (aflibercept-boav) injection, 2 mg (0.05 mL of 40 mg/mL) in a single-dose vial (vial kit), for intravitreal use as a proposed (b) (4) biosimilar to U.S.-licensed Eylea (aflibercept) 2 mg (0.05 mL of 40 mg/mL) injection in a vial kit for intravitreal use,
- Eydenzelt (aflibercept-boav) injection, 2 mg (0.05 mL of 40 mg/mL) in a single-dose vial (vial kit), for intravitreal use as a proposed (b) (4) biosimilar to U.S.-licensed Eylea (aflibercept) 2 mg (0.05 mL of 40 mg/mL) injection in a single-dose prefilled syringe (PFS) for intravitreal use,
- Eydenzelt (aflibercept-boav) injection, 2 mg (0.05 mL of 40 mg/mL) in a PFS, for intravitreal use as a proposed (b) (4) biosimilar to U.S.-licensed Eylea (aflibercept) 2 mg (0.05 mL of 40 mg/mL) injection in a PFS, for intravitreal use, and
- Eydenzelt (aflibercept-boav) injection, 2 mg (0.05 mL of 40 mg/mL) in a PFS, for intravitreal use as a proposed biosimilar to U.S.-licensed Eylea (aflibercept) 2 mg (0.05 mL of 40 mg/mL) injection in a vial kit, for intravitreal use.

(b) (4)

For administrative purposes, we have split BLA 761377 as follows:

- BLA 761377/Original 1 – biosimilarity [redacted] (b) (4)

The subject of this correspondence is BLA 761377/Original 1. [redacted] (b) (4)

All future submissions to these BLAs should specify the BLA number and the Original number to which each submission pertains.

LICENSING

We have approved your BLA for Eydenzelt (aflibercept-boav), effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Eydenzelt under your existing Department of Health and Human Services U.S. License No. 1996. Eydenzelt 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 Eydenzelt drug substance at Celltrion Inc. (Plant I), in Incheon, Republic of Korea. The final formulated drug product will be manufactured, prefilled in syringe, labeled, and packaged at [redacted] (b) (4) The final formulated drug product will be manufactured, filled in vial, labeled, and packaged at [redacted] (b) (4) You may label your product with the proprietary name, Eydenzelt, and market it in 2 mg/0.05 mL (40 mg/mL) prefilled syringe or 2 mg/0.05 mL (40 mg/mL) single-dose vial for intravitreal use.

DATING PERIOD

The dating period for Eydenzelt prefilled syringe shall be 24 months from the date of manufacture when stored at 2°C to 8°C. The dating period for Eydenzelt vial presentation shall be 36 months from the date of manufacture when stored at 2°C to 8°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 [redacted] (b) (4) months from the date of manufacture when stored at [redacted] (b) (4) °C.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Eydenzelt 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 Eydenzelt, 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.

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 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 761377/Original 1**." 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We have determined that, at this time, no pediatric studies will be required under PREA for your BLA.

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]

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

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 601.12(f)(4)]. 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, contact Dheera Semidey, Senior Regulatory Project Manager, at Dheera.Semidey@fda.hhs.gov or call 301-796-3009.

Sincerely,

{See appended electronic signature page}

William Boyd, MD
Deputy Director
Division of Ophthalmology
Office of Specialty Medicine
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- 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/

WILLIAM M BOYD
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