CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761378Orig1s000

Trade Name:	AHZANTIVE injection, for intravitreal use
Generic or Proper Name:	*aflibercept-mrbb*
Sponsor:	Formycon AG
Approval Date:	June 28, 2024
Indication:	*AHZANTIVE is a vascular endothelial growth factor (VEGF) inhibitor indicated for the treatment of patients with:* • *Neovascular (Wet) Age-Related Macular Degeneration (AMD)* • *Macular Edema Following Retinal Vein Occlusion (RVO)* • *Diabetic Macular Edema (DME)* • *Diabetic Retinopathy (DR)*

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APPLICATION NUMBER:

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APPROVAL LETTER

BLA 761378/Original 1

BLA APPROVAL

Formycon AG
c/o Strategic Drug Development Services, LLC
Attention: Scott A. Oglesby, PhD
Principal Consultant
6518 Green Rise Road
Hillsborough, NC 27278

Dear Dr. Oglesby:

Please refer to your biologics license application (BLA) dated and received June 28, 2023, and your amendments, under section 351(k) of the Public Health Service Act for Ahzantive (aflibercept-mrbb) injection.

This BLA seeks licensure of Ahzantive (aflibercept-mrbb) 2 mg (0.05 mL of 40 mg/mL) injection, for intravitreal use in a single-dose vial (vial) (b) (4) US-Eylea (aflibercept) 2 mg (0.05 mL of 40 mg/mL) injection, for intravitreal use in a vial kit and single-dose pre-filled syringe (PFS).
Ahzantive seeks licensure (b) (4) US-Eylea for the following indications:

- Neovascular (wet) Age-Related Macular Degeneration (AMD)
- Macular Edema Following Retinal Vein Occlusion (RVO)
- Diabetic Macular Edema (DME)
- Diabetic Retinopathy (DR)

For administrative purposes, we have split BLA 761378 into the following applications:

- BLA 761378/Original 1 – Ahzantive (aflibercept-mrbb):
    - Ahzantive 2 mg (0.05 mL of 40 mg/mL) injection, for intravitreal use in a vial seeking biosimilarity to US-Eylea 2 mg (0.05 mL of 40 mg/mL) injection, for intravitreal use in a vial kit and PFS.

(b) (4)

The subject of this action letter is BLA 761378/Original 1. [redacted]

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

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2322 to Formycon AG, Martinsried/Planegg, Bavaria, Germany, under the provisions of section 351(k) 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 Ahzantive (aflibercept-mrbb). Ahzantive is indicated for the treatment of neovascular (wet) age-related macular degeneration (AMD), macular edema following retinal vein occlusion (RVO), diabetic macular edema (DME), and diabetic retinopathy (DR).

MANUFACTURING LOCATIONS

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

DATING PERIOD

The dating period for Ahzantive shall be 24 months from the date of manufacture when stored at 2°C - 8°C, 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 [redacted] months from the date of manufacture when stored [redacted]

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Ahzantive 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 Ahzantive, 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 AND 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, as described at FDA.gov.[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.*[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 *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 761378/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

[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.

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]

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 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 for licensed biological products (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 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:

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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

If you have any questions, call Kidist Berhanu, Regulatory Project Manager, at (301) 837-7665.

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

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/

WILLIAM M BOYD
06/28/2024 03:11:57 PM