CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761197Orig1s000

Trade Name:	SUSVIMO
Generic or Proper Name:	ranibizumab injection, for intravitreal use via SUSVIMO ocular implant
Sponsor:	Genentech, Inc.
Approval Date:	October 22, 2021
Indication:	For the treatment of patients with Neovascular (wet) Age-related Macular Degeneration (AMD)

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APPROVAL LETTER

BLA 761197

BLA APPROVAL

Genentech, Inc.
Attention: Meike Lorenz-Candlin, PhD
Regulatory Program Management
1 DNA Way
South San Francisco, CA 94080

Dear Dr. Lorenz-Candlin:

Please refer to your biologics license application (BLA) dated and received April 23, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for SUSVIMO (ranibizumab injection), 100mg/mL in a single-dose vial.

LICENSING

We have approved your BLA for SUSVIMO (ranibizumab injection) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Susvimo under your existing Department of Health and Human Services U.S. License No. 1048. Susvimo is indicated for the treatment of patients with Neovascular (wet) Age-related Macular Degeneration (AMD).

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture ranibizumab drug substance at Roche Singapore Technical Operations Ltd., in Singapore, Singapore. The final formulated ranibizumab drug product will be manufactured and filled (b) (4) (b) (4) The filled ranibizumab drug product will be labeled, packaged, and co-packaged with the Initial Fill Needle at Genentech, Inc., in Hillsboro, Oregon. The Port Delivery System device constituent parts will be manufactured, packaged and labeled (b) (4) (b) (4) You may label your product with the proprietary name, SUSVIMO, and market it as a 100 mg/mL solution with10 mg in 0.1 mL contained in single-dose vial.

DATING PERIOD

The dating period for Susvimo shall be 24 months from the date of manufacture when stored at 2-8°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 (b) (4) months from the date of manufacture when stored at (b) (4) °C. The dating period for the Initial Fill Needle is (b) (4) months from the date of manufacture when stored at (b) (4) (b) (4) °C.

The expiration date for the co-packaged product, Susvimo (ranibizumab injection) plus Initial Fill Needle shall be on the earliest expiration date of any component.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of ranibizumab 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 Susvimo (ranibizumab injection) 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 SUSVIMO, 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 text for the Prescribing Information, Instructions for Use, and Medication Guide. 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: enclosed carton and container labeling, as soon as they are available, but no more than 30 days after

[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.

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 761197**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for ranibizumab injection was not referred to an FDA advisory committee because this biologic is not first in its 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 necessary studies are impossible or highly impracticable because there are too few pediatric patients with Age Related Macular Degeneration to study.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct post-marketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute. We have determined that an analysis of spontaneous post-marketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected risk of corneal endothelial cell loss. The active post-market risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk. We have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to identify an unexpected risk of corneal endothelial cell loss. Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following trials:

4157-2 Conduct a controlled trial in which the health of the corneal endothelial cells are evaluated by monitoring the number/density of corneal endothelial cells over a period of at least one year in at least 100 patients receiving the 100 mg/mL ranibizumab administered through the Port Delivery System.

The timetable you submitted on October 14, 2021, states that you will conduct this trial according to the following schedule:

Final Protocol Submission: 1/2022
Trial Completion: 12/2024
Final Report Submission: 5/2025

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Submit clinical protocol(s) to your IND 113552 with a cross-reference letter to this BLA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **Required Post-marketing Protocol Under 505(o), Required Post-marketing Final Report Under 505(o), Required Post-marketing Correspondence Under 505(o).**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 601.70 requires you to report annually on the status of any post-marketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 601.70. We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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

We remind you of your post-marketing commitments:

4157-1 Perform real-time Susvimo drug product commercial container closure system leachable studies using appropriate test methods to identify and quantify volatile organic compounds (VOC), semi-VOC, and non-VOC, and elemental impurities at regular intervals through the end of shelf-life. The leachables results will be updated annually in the BLA Annual Report. The final results of this study and the toxicological risk evaluation for the levels of leachates detected in the drug product will be provided in the final study report to the BLA.

The timetable you submitted on October 4, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 3/2023

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. 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*.[4]

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

[4] 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.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

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:

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 post-marketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product post-marketing safety reporting is available at FDA.gov.[7]

[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf
[7] https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products

POST APPROVAL FEEDBACK MEETING

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 Lois Almoza, Senior Regulatory Project Manager, at (240)402-5146.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Director
Division of Ophthalmology
Office of Specialty Medicine
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use
- 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/

WILEY A CHAMBERS
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