CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

125387Orig1s000

Trade Name: Eylea

Generic Name: aflibercept

Sponsor: Regeneron Pharmaceuticals Inc.

Approval Date: November 18, 2011

Indications: Treatment of neovascular (wet) age-related macular degeneration.

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

Our STN: BL 125387/0

BLA APPROVAL
November 18, 2011

Regeneron Pharmaceuticals, Inc.
Attention: Laura Pologe, Ph.D.
Associate Director, Regulatory Affairs
777 Old Saw Mill River Road
Tarrytown, New York 10591-6707

Dear Dr. Pologe:

Please refer to your Biologics License Application (BLA) dated February 17, 2011, received February 18, 2011, submitted under section 351 of the Public Health Service Act for Eylea (aflibercept).

We acknowledge receipt of your amendments dated February 28, March 10, 18, and 24, April 1, 8, 11 (two), 13 (two), and 29, May 11, 16, 23, and 27, June 3, 7, 9, 16, 20, and 28, July 8, 18, and 19, August 1, 5, 10, 12, and 31, September 1, 7, 12, 20, and 26, October 7, 21, 24, and 27, and November 1, 9, 11, and 17, 2011.

We have approved your BLA for aflibercept effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, aflibercept under your existing Department of Health and Human Services U.S. License No. 1760. Aflibercept is indicated for treatment of neovascular (wet) age-related macular degeneration.

Under this license, you are approved to manufacture aflibercept drug substance intermediate, drug substance, and formulated bulk at (b) (4). The final formulated drug product will be manufactured at (b) (4) The final formulated drug product will be labeled and packaged at (b) (4). You may label your product with the proprietary name Eylea and market it in a (b) (4) single-use vial containing 0.278 mL of 40 mg/mL aflibercept, as part of a final packaged product containing the aflibercept single-use vial, a 19-gauge x 1½-inch 5-micron filter needle, a 30-gauge x ½-inch needle and a 1-mL plastic syringe.

The dating period for aflibercept shall be 15 months from the date of manufacture when stored at 2 - 8°C. The date of manufacture shall be defined as the (b) (4) The expiration date for the packaged product, (aflibercept single-use vials, syringe, needle and filter needle) shall be dependent on the shortest expiration date of any component. (b) (4)

(b) (4)

Results of ongoing stability should be submitted to the annual report.

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

We are approving this application for use as recommended in the enclosed agreed-upon labeling text.

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 [21 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA STN 125387**."

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels submitted on November 17, 2011, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)". Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved BLA STN 125387**." Approval of this submission by FDA is not required before the labeling is used.

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