BLA 125418/S-046

SUPPLEMENT APPROVAL

sanofi-aventis, U.S., LLC
Attention: Stefanie Doty
Senior Director, Regulatory Affairs
55 Corporate Drive
Mail Stop: 55C-300
Bridgewater, NJ 08807

Dear Ms. Doty:

Please refer to your supplemental biologics license application (sBLA), dated and received August 14, 2019, and your amendments, submitted under section 351(a) of the Public Health Service Act for Zaltrap (ziv-aflibercept) injection, 100 mg/4mL and 200 mg/8mL.

This Prior Approval supplemental biologics application provides for updates to the approved labeling to:

- remove the Boxed WARNINGS for Hemorrhage, Gastrointestinal Perforation, and Compromised Wound Healing;
- add information to the Highlights section under WARNINGS AND PRECAUTIONS for the Hemorrhage, Gastrointestinal Perforation, and Impaired Wound Healing subsections;
- revise the subsection title for WARNINGS AND PRECAUTIONS, Impaired Wound Healing (5.3) and clarify the directions for withholding Zaltrap prior to elective surgery and for the timing of resumption after major surgery; and
- revise the PATIENT COUNSELING (17) section for consistency with WARNINGS AND PRECAUTIONS, Impaired Wound Healing (5.3).

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, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in Microsoft Word format that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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 indications 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.

PROMOTIONAL MATERIALS

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 601.12(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4) to the address above, by fax to 301-847-8444, or electronically in

[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 https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Kwadwo Korsah, Pharm.D., Regulatory Health Project Manager, at (301) 796-6630.

Sincerely,

{See appended electronic signature page}

Patricia Keegan, M.D.
Acting Associate Director of Medical Policy
Oncology Center of Excellence
U.S. Food and Drug Administration

ENCLOSURE(S):

- Content of 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/

PATRICIA KEEGAN
03/11/2020 11:31:06 AM