BLA 761113/S-011

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING REQUIREMENT

Sanofi-Aventis US LLC
Attention: Allan Bonsol
Director, Regulatory Affairs
450 Water Street
Cambridge, MA 02141

Dear Allan Bonsol:

Please refer to your supplemental biologics license application (sBLA), submitted and received on January 26, 2024, and your amendments, submitted under section 351(a) of the Public Health Service Act for Sarclisa (isatuximab-irfc), injection.

This Prior Approval Supplemental (PAS) biologics license application provides for updates to the US Prescribing Information including:

- Section 14 Clinical Studies – updated with the overall survival data from Study EFC15246 (IKEMA)
- Section 5 Warnings and Precautions, 5.3 Second Primary Malignancies – revised rates of second primary malignancies
- Section 5 Warnings and Precautions, Section 5.4, Laboratory Test Interference – updated to identify the time period for the detection of interference with serological testing
- Section 12 Clinical Pharmacology, Section 12.3, Pharmacokinetics, Special Populations – updated the exposure of isatuximab on renal impairment
- Section 17, Patient Counseling – updated to advise patients that Sarclisa may affect results of blood tests to match blood type for approximately 6 months following last infusion

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.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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, Patient Package Insert) 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 indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your supplement application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated September 29, 2023, containing the final report for the following postmarketing requirement listed in the March 31, 2021, approval letter for BLA 761113/S-003.

[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.

4040-1 Conduct a clinical trial sufficient to characterize and determine the incidence of second primary malignancies in patients receiving isatuximab in combination with carfilzomib and dexamethasone (Isa-Kd). This data may come from Study EFC15246 (IKEMA). Include incidence rates, time to onset, outcomes, and efficacy in the final report. Efficacy should include final progression-free survival and overall survival results.

We have reviewed your submission and conclude that the above requirement was fulfilled.

We remind you that there is a postmarketing commitment listed in the March 31, 2021, letter that is still open.

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]

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety- related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related 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 314.70(a)(4).

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).

[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

If you have any questions, call Kimberly Scott, Senior Regulatory Health Project Manager, at (240) 402-4560.

Sincerely,

{See appended electronic signature page}

Bindu Kanapuru, MD
Associate Director for Therapeutic Review
Division of Hematologic Malignancies II
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

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/

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