



BLA 761113/S-009

**SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING REQUIREMENT/COMMITMENTS**

Sanofi-Aventis US LLC.
c/o Sanofi US Services Inc.
Attention: Patricia M. Johnson
North America Regulatory Affairs
Therapeutic Lead, Oncology
450 Water Street
Cambridge, MA 02142

Dear Patricia Johnson:

Please refer to your supplemental biologics license application (sBLA), dated and received January 26, 2023, submitted under section 351(a) of the Public Health Service Act for Sarclisa (isatuximab-irfc) injection.

This Prior Approval supplemental biologics license application provides for updating the US Prescribing Information (USPI) Patient Package Insert (PPI) for Sarclisa to include the following updates:

- Section 14 Clinical Studies – added final overall survival data from study EFC14335 (ICARIA) (PMR 3782-3) and the final progression free survival efficacy data from study EFC15246 (IKEMA).
- Section 5 Warnings and Precautions - updated the rate of second primary malignancies from the IKEMA study.
- Section 7.1 Laboratory Test Interference – updated to provide guidance on usage of the FDA cleared isatuximab-irfc specific assay
- Updates to the Patient Package Insert to align with the USPI.

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

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT/COMMITMENTS

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>.

We have received your submissions dated August 31, 2021, and October 19, 2022, containing the final reports for the following postmarketing requirement/commitments listed in the March 2, 2020, approval letter for BLA 761113.

- 3782-1 Conduct long term safety monitoring of patients enrolled in study (ICARIA) titled; “A Phase 3 Randomized, Open-label, Multicenter Study Comparing Isatuximab (SAR650984) in Combination With Pomalidomide and Low-Dose Dexamethasone Versus Pomalidomide and Low-Dose Dexamethasone in Patients With Refractory or Relapsed and Refractory Multiple Myeloma”, to determine the incidence of acute myeloid leukemia, myelodysplastic syndrome and other second primary malignancies in patients receiving isatuximab in combination with pomalidomide and dexamethasone and its potential to have a detrimental impact on overall survival. Include incidence rates, time to onset, predisposing factors, and outcomes with the final report.

- 3782-3 Submit the overall survival analysis and datasets with the final report for clinical trial (ICARIA) titled; “A Phase 3 Randomized, Open-label, Multicenter Study Comparing Isatuximab (SAR650984) in Combination With Pomalidomide and Low-Dose Dexamethasone Versus Pomalidomide and Low-Dose Dexamethasone in Patients With Refractory or Relapsed and Refractory Multiple Myeloma” to provide additional long term efficacy data that may inform product labeling.

- 3782-4 Develop a validated assay to detect interference of isatuximab to any remaining endogenous M protein in the patient’s serum, to facilitate determination of a complete response (CR) in patients with multiple myeloma. Complete and submit the final report of the validation study, that may provide information to prescribers about the use of the assay to determine CR.

We have reviewed your submissions and conclude that the above requirement/commitments were fulfilled.

We remind you that there is a postmarketing requirement listed in the March 2, 2020, approval 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

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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

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 Kimberly Scott, Senior Regulatory Health Project Manager, at (240) 402-4560.

Sincerely,

{See appended electronic signature page}

Nicole Gormley, MD
Director
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

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>

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/

NICOLE J GORMLEY
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