

BLA 761324/S-009

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT**

Genmab US, Inc.
Attention: Sachin Patel, PharmD, MBA, RPh
Associate Director, Global Regulatory Affairs
777 Scudders Mill Road
Bldg 2, 4th Floor
Plainsboro, NJ 08536

Dear Dr. Patel:

Please refer to your supplemental biologics license application (sBLA) dated and received May 30, 2025, and your amendments, submitted under section 351(a) of the Public Health Service Act for Epkinly (epcoritamab-bysp) injection.

This Prior Approval supplemental biologics license application provides for the following:

- new indication for Epkinly in combination with lenalidomide and rituximab for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL).
- conversion to traditional approval for the following indication: Epkinly as monotherapy for the treatment of adult patients with relapsed or refractory FL after two or more lines of systemic therapy.

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](http://www.fda.gov),¹ that is identical to the enclosed labeling (text for the Prescribing Information and Medication Guide) and include the labeling changes proposed in any pending “Changes Being Effectuated” (CBE) supplements.

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

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).

SUBPART E FULFILLED

We approved this BLA under the regulations at 21 CFR 601 Subpart E for Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 601.41.

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

We have received your submission dated May 31, 2025, containing the final report for the following postmarketing requirement listed in the June 26, 2024, approval letter for BLA 761324/S-003.

- 4657-1 Complete a randomized clinical trial intended to verify and describe the clinical benefit of epcoritamab in patients with relapsed or refractory follicular lymphoma. Patients should be randomized to receive

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>.

epcoritamab in combination with rituximab and lenalidomide versus rituximab and lenalidomide. The primary endpoint should be progression-free survival, with overall survival as a secondary endpoint. The trial should enroll a sufficiently representative study population that reflects the racial and ethnic diversity of the U.S. population of patients with follicular lymphoma and allow for interpretation of the results in these populations.

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

We remind you that there is postmarketing requirement listed in the June 26, 2024, 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

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 601.12(f)(4)]. 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 601.12(f)(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 601.12(f)(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 Natasha Kormanik, Senior Regulatory Project Manager, at (240) 402-4227 or Natasha.Kormanik@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Bindu Kanapuru, MD
Deputy Division Director (Acting)
Division of Hematologic Malignancies II
Office of Oncologic Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Medication Guide

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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