BLA 761334/S-004

SUPPLEMENT APPROVAL

Incyte Corporation
Attention: Felicia Diggs, RN, BSN, MSN
Associate Director, Global Regulatory Affairs
1801 Augustine Cut-Off
Wilmington, DE 19803

Dear Felicia Diggs:

Please refer to your supplemental biologics license application (sBLA) received December 19, 2024, and your amendments, submitted under section 351(a) of the Public Health Service Act for Zynyz (retifanlimab-dlwr) injection, for intravenous use.

This Prior Approval supplemental biologics license application proposes to add new indications for Zynyz (retifanlimab-dlwr):

- In combination with carboplatin and paclitaxel for the first-line treatment of adult patients with metastatic or with inoperable locally recurrent squamous cell carcinoma of the anal canal (SCAC).

- As a single agent for the treatment of adult patients with locally recurrent or with metastatic SCAC with disease progression on or intolerance to platinum-based chemotherapy.

APPROVAL

We have completed our review of this sBLA, as amended. This supplement is approved.

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 Medication Guide) 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.

[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.

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

4839-1 Complete the ongoing randomized clinical trial, INCMGA 0012-303 (NCT04472429), entitled "A Phase 3 Global, Multicenter, Double-Blind Randomized Study of Carboplatin-Paclitaxel With INCMGA00012 or Placebo in Participants With Inoperable Locally Recurrent or Metastatic Squamous Cell Carcinoma of the Anal Canal Not Previously Treated With Systemic Chemotherapy (POD1UM-303/InterAACT 2)" and provide the final overall survival analysis to further characterize the efficacy of retifanlimab in combination with systemic chemotherapy for the treatment of inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal.

The timetable you submitted on April 17, 2025, states that you will conduct this study according to the following schedule:

Trial Completion:	09/2026
Final Report Submission:	03/2027

Submit the datasets with the final report submission.

Submit clinical protocols to your IND 139333 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

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]

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

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).

If you have any questions, email Autumn Zack-Taylor, MS, Senior Regulatory Health Project Manager, at Autumn.Zack-Taylor@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Steven Lemery, MD, MHS
Director
Division of Oncology 3
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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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/

STEVEN J LEMERY
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