BLA 761381/S-005

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING REQUIREMENT/
RELEASE OF POSTMARKETING REQUIREMENT

Bristol-Myers Squibb Company
Attention: Jateh Major, PharmD
Associate Director, Global Regulatory Sciences and Policy, Oncology
P.O. Box 5326
Princeton, NJ 08543-5326

Dear Dr. Major:

Please refer to your January 30, 2025, supplemental biologics license application (sBLA) and your amendments, submitted under section 351(a) of the Public Health Service Act for Opdivo Qvantig (nivolumab and hyaluronidase-nvhy), subcutaneous injection.

This Prior Approval supplemental biologics license expands the current melanoma and unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer indications in product labeling to allow for use in pediatric patients 12 years of age and older.

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.

This supplement provides for pediatric labeling text pursuant to the Pediatric Research Equity Act (PREA) in response to a PREA PMR.

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.

[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).

CARTON AND CONTAINER LABELING

We acknowledge your January 30, 2025, submission containing final printed carton and container labeling.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on January 30, 2025, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761381/S-005**." Approval of this submission by FDA is not required before the labeling is used.

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.

[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 note that you have fulfilled the pediatric study requirement for patients 12 years of age and older for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated January 30, 2025, containing the final report for the following postmarketing requirement listed in the October 27, 2025, approval letter for BLA 761381/S-002.

4925-1 Conduct a modeling and simulation study to support dosing of nivolumab and hyaluronidase-nvhy as first-line treatment in pediatric patients 12 years of age and older with unresectable or metastatic microsatellite instability-high or mismatch repair deficient colorectal cancer (MSI-H/dMMR mCRC).

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

This closes all of your postmarketing requirements and postmarketing commitments acknowledged in our October 27, 2025, letter. You are not required to report on the status of closed (released or fulfilled) PMRs/PMC in your annual report required under 21 CFR 601.70.

RELEASE OF POSTMARKETING REQUIREMENT

We have received your submission dated January 30, 2025, related to the following postmarketing requirement listed in our December 27, 2024, approval letter:

4762-4 Conduct a molecularly targeted pediatric cancer investigation using an age-appropriate formulation of nivolumab and hyaluronidase-nvhy in pediatric patients 12 years of age and older.

Final Report Submission: 01/2025

We have reviewed your submission and have determined that you are released from the above requirement as it is no longer needed because you have provided the necessary information to support dosing of an age-appropriate formulation of nivolumab and hyaluronidase-nvhy in pediatric patients 12 years of age and older.

We remind you that there is a postmarketing commitment listed in the December 27, 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).

If you have any questions, contact Gina Davis, Senior Regulatory Health Project Manager at Gina.Davis@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

[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

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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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