BLA 125554/S-127

SUPPLEMENT APPROVAL

Bristol-Myers Squibb Company
Attention: Shrutti Saggi
Executive Director, Oncology
PO Box 5326
Princeton, NJ 08543

Dear Shrutti Saggi:

Please refer to your supplemental biologics license application (sBLA), dated December 8, 2023, received December 8, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for Opdivo (nivolumab) injection.

This Prior Approval supplemental biologics license application provides for the use of Opdivo, in combination with platinum-doublet chemotherapy, for the neoadjuvant treatment of adult patients with resectable (tumors ≥4 cm or node positive) non-small cell lung cancer and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements, followed by single-agent Opdivo as adjuvant treatment after surgery.

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 HIGHLIGHTS 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 (Prescribing Information and

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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.

We are waiving the pediatric study(ies) requirement for this application because necessary studies are impossible or highly impracticable in non-small cell lung cancer.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4711-1 Complete the ongoing clinical trial, CheckMate 77T (CA20977T, NCT04025879), and analyze the final overall survival (OS) once the required 174 events for the OS endpoint have occurred, to further characterize the clinical benefit of nivolumab in combination with platinum-containing chemotherapy as neoadjuvant treatment, followed by nivolumab continued as a single agent as adjuvant treatment after surgery for adults with resectable (tumors ≥4 cm or node positive) non-small cell

[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.

lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

The timetable you submitted on October 1, 2024, states that you will conduct this study according to the following schedule:

Trial Completion:	10/2026
Final Report Submission:	04/2027

Submit the datasets with the final report submission.

4711-2 Conduct an integrated analysis of completed, ongoing, and planned trials of perioperative nivolumab for patients with resectable non-small cell lung cancer (NSCLC) to evaluate the contribution of phase of nivolumab when given in combination with platinum-containing chemotherapy as neoadjuvant treatment and continued as a single agent as adjuvant treatment after surgery for adults with resectable (tumors ≥4 cm or node positive) NSCLC and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements. This analysis should also include an evaluation of safety, including immune-mediated adverse reactions that occur during each phase of treatment.

The timetable you submitted on October 1, 2024, states that you will conduct this study according to the following schedule:

Draft Protocol Submission (Analysis Plan):	01/2025
Final Protocol Submission (Analysis Plan):	07/2025
Study Completion:	10/2026
Final Report Submission:	04/2027

4711-3 Conduct an integrated analysis of data from clinical trials and observational studies (e.g., real world evidence), post-marketing reports, and other sources to further characterize the safety and efficacy/effectiveness of the perioperative nivolumab regimen in older adults ages 75 years and older and patients of underrepresented racial and ethnic minority groups with non-small cell lung cancer (NSCLC). The analyses should support an evaluation of comparative efficacy/effectiveness and safety between the population primarily represented in the trial (CheckMate77T trial) and the aforementioned underrepresented racial and ethnic minority population as well as the aforementioned older adult population and younger patients represented in CheckMate77T.

The timetable you submitted on October 1, 2024, states that you will conduct this study according to the following schedule:

Draft Protocol Submission (Analysis Plan):	01/2025
Final Protocol Submission (Analysis Plan):	07/2025
Study Completion:	03/2028
Final Report Submission:	09/2028

A final submitted protocol is one that the FDA has reviewed and commented upon and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 100052 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]

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]

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, contact Jeffrey Ingalls, Regulatory Health Project Manager, at 301-796-4444 or via email at Jeffrey.Ingalls@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Erin Larkins, MD
Director (Acting)
Division of Oncology 2
Office of Oncologic Diseases
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/

ERIN A LARKINS
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