BLA 125514/S-188

SUPPLEMENT APPROVAL

Merck Sharp & Dohme LLC
Attention: Nupur Mittal
126 East Lincoln Avenue
P.O. Box 2000, RY34B-332
Rahway, NJ 07065

Dear Nupur Mittal:

Please refer to your supplemental biologics license application (sBLA) received October 7, 2025, and your amendments, submitted under section 351(a) of the Public Health Service Act for Keytruda (pembrolizumab) intravenous injection.

This Prior Approval supplemental biologics license application provides for a new indication for Keytruda, in combination with enfortumab vedotin, as neoadjuvant treatment, and then continued after cystectomy as adjuvant treatment for the treatment of adult patients with muscle invasive bladder cancer who are ineligible for cisplatin-containing chemotherapy.

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 (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]

[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.

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 requirement for this application because studies would be impossible or highly impracticable.

POSTMARKETING COMMITMENT SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

4396-1 Complete the ongoing clinical trial, KEYNOTE-905/EV-303 (NCT03924895), titled "Perioperative Pembrolizumab (MK-3475) Plus Cystectomy or Perioperative Pembrolizumab Plus Enfortumab Vedotin Plus Cystectomy Versus Cystectomy Alone in Participants Who Are Cisplatin-ineligible or Decline Cisplatin With Muscle-invasive Bladder Cancer", and provide the pre-planned final overall survival analysis, to further characterize the clinical benefit of pembrolizumab in combination with enfortumab vedotin as neoadjuvant treatment, and then continued after radical cystectomy as adjuvant treatment for the treatment of adult patients with muscle invasive bladder cancer who are ineligible for or declined cisplatin-containing chemotherapy.

The timetable you submitted on November 10, 2025, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 01/2025 (completed)
Trial Completion: 06/2028
Final Report Submission: 12/2028

Submit any clinical protocols or amendments for the above trial to your IND 122753 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 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]

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 Alice Lee, Senior Regulatory Project Manager, at (301) 796-8881 or at Alice.Lee@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Daniel Suzman, MD
Deputy Director
Division of Oncology 1
Office of Oncologic Diseases
Center for Drug Evaluation and Research

[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

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/

DANIEL L SUZMAN
11/21/2025 10:33:52 AM