BLA 761495

BLA APPROVAL

Merck Sharp & Dohme LLC
Attention: Janice Kim, PharmD, MS
Director, Global Regulatory Affairs
126 East Lincoln Avenue, P.O. Box 2000
RY34-A2014
Rahway, NJ 07065

Dear Dr. Kim:

Please refer to your biologics license application (BLA) received July 11, 2025, and your amendments, submitted under section 351(a) of the Public Health Service Act for Keytruda Qlex (pembrolizumab and berahyaluronidase alfa-pmph) injection, for subcutaneous use.

LICENSING

We have approved your BLA for Keytruda Qlex (pembrolizumab and berahyaluronidase alfa-pmph) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce Keytruda Qlex, under your existing Department of Health and Human Services U.S. License No. 0002. Keytruda Qlex is indicated for the treatment of adult patients with resectable locally advanced head and neck squamous cell cancer (HNSCC) whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, as a single agent as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without cisplatin and then as a single agent.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Keytruda Qlex (pembrolizumab 165 mg/ml) drug substance at (b) (4) and berahyaluronidase alfa drug substance at (b) (4) The final formulated drug product will be manufactured, filled, labeled at (b) (4), and packaged at Merck Sharp & Dohme LLC, Wilson, North Carolina (FEI: 1036761), and Merck Sharp & Dohme B.V., Haarlem, Netherlands (FEI: 3002807658). You may label your product with the proprietary name, Keytruda Qlex, and market it in 2.4 mL (395 mg pembrolizumab and 4800 units berahyaluronidase alfa) and 4.8 mL (790 mg pembrolizumab and 9600 units berahyaluronidase alfa) (b) (4) glass vials as solution for injection for subcutaneous administration.

DATING PERIOD

The dating period for Keytruda Qlex shall be 24 months from the date of manufacture when stored at 5 ± 3 °C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your pembrolizumab 165 mg/ml drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) The dating period for your berahyaluronidase alfa drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4)

We have approved the stability protocol(s) in your license application for the purpose of extending the expiration dating period of your berahyaluronidase alfa drug substance and drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Keytruda Qlex to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Keytruda Qlex, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

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.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide). Information on submitting SPL files using eLIST may be found in the

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

guidance for industry *SPL Standard for Content of Labeling Technical Qs and As (October 2009)*.[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, 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 *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761495**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for pembrolizumab and berahyaluronidase alfa-pmph was not referred to an FDA advisory committee because outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

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 all pediatric age groups because necessary studies are impossible or highly impracticable. This is due to the rarity of the disease in this population.

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-*

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements at 21 CFR 600.81.

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

We have now administratively closed this BLA. Therefore, carton and container final

[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

printed labeling (if requested above), all 15-day alert reports, periodic (including quarterly) adverse drug experience reports, field alerts, annual reports, supplements, promotional materials and other submissions should be addressed to the parent **BLA 761467** for this product, not to this BLA. **In the future, do not make submissions to this BLA**.

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

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

Sincerely,

{See appended electronic signature page}

Paz Vellanki, MD, PhD
Supervisory Associate Director (Acting)
Office of Oncologic Disease
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- 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/

PAZ J VELLANKI
10/15/2025 03:27:00 PM