BLA 761232

BLA APPROVAL

BeiGene U.S.A., Inc.
Attention: Chandra Vemavarapu, Ph.D.
Senior Director, Regulatory Affairs
1840 Gateway Drive, 3rd Floor
San Mateo, CA 94404

Dear Dr. Vemavarapu:

Please refer to your biologics license application (BLA) dated July 10, 2021, received July 12, 2021, submitted under section 351(a) of the Public Health Service Act for Tevimbra (tislelizumab-jsgr) injection, for intravenous use.

We also refer to our June 21, 2022, advice letter wherein we informed you of the delay in conducting facility inspections due to COVID travel restrictions and that inspections of the (b) (4) drug substance and drug product manufacturing facility (b) (4) and of the BeiGene (Suzhou) Co., Ltd. testing facility (FEI: 3014150588) would be required before the application could be approved.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2232 to BeiGene U.S.A., Inc., San Mateo, California, under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product Tevimbra (tislelizumab-jsgr). Tevimbra, as a single agent, is indicated for the treatment of adult patients with unresectable or metastatic esophageal squamous cell carcinoma after prior systemic chemotherapy that did not include a PD-(L)1 inhibitor.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture tislelizumab-jsgr at your facility in Shanghai, China. You may label your product with the proprietary name, Tevimbra, and market it as 100 mg/10 mL (10 mg/mL) injection in a single-dose vial.

DATING PERIOD

The dating period for Tevimbra shall be 36 months from the date of manufacture when stored at 5°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 drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4).

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Tevimbra 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 Tevimbra, 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 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.

[1] See 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 at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

CARTON AND CONTAINER LABELING

We acknowledge your January 9, 2024, submission containing final printed carton and container labeling.

ADVISORY COMMITTEE

Your application for Tevimbra was not referred to an FDA advisory committee because the application did not raise significant public health questions on the role of the biologic in the diagnosis, cure, mitigation, treatment, or prevention of a disease.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4576-1 Develop a reliable endotoxin detection method that can overcome the LER phenomenon for the tislelizumab drug product.

The timetable you submitted on 01/18/2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/31/2024

4576-2 Implementation of in-line pressure monitoring of sterile filtration.

The timetable you submitted on 01/18/2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 05/31/2024

Submit clinical protocols to your IND 135699 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**."

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 studies requirement for this application because this product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is not likely to be used in a substantial number of pediatric patients. There is no scientific rationale for pediatric patients to be enrolled in new monotherapy clinical studies of additional anti-PD-(L)1 antibodies with the same mechanism of action of agents already studied. The waiver was requested in all pediatric patients based on the rationale that there is no convincing evidence that tislelizumab-jsgr (an anti-PD-1 antibody) provides superior pharmacologic, toxicity, or activity profile to the same in class products already studied.

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

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.

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[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

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

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 Rebecca Cohen, Regulatory Health Project Manager, at (240) 402-4998.

Sincerely,

{See appended electronic signature page}

Paul G Kluetz, M.D.
Supervisory Associate Director (acting)
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

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

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/

REBECCA L COHEN
03/13/2024 03:54:59 PM

PAUL G KLUETZ
03/14/2024 11:12:59 AM