CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761417Orig1s000

Trade Name:	Tevimbra injection for intravenous use.
Generic or Proper Name:	tislelizumab-jsgr
Sponsor:	BeiGene U.S.A., Inc
Approval Date:	December 26, 2024
Indication:	Tevimbra is indicated, in combination with platinum and fluoropyrimidine based chemotherapy, for the first-line treatment of adults with unresectable or metastatic HER2-negative gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 (≥1).

CENTER FOR DRUG EVALUATION AND RESEARCH

761417Orig1s000

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	**X**
Other Action Letters	
Labeling	**X**
REMS	
Officer/Employee List	**X**
Multidiscipline Review(s)	**X**
Product Quality Review(s)	**X**
Clinical Microbiology / Virology Review(s)	
Other Reviews	**X**
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	**X**
Administrative/Correspondence Document(s)	**X**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761417Orig1s000

APPROVAL LETTER

BLA 761417

BLA APPROVAL

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

Dear Dr. Ledoux:

Please refer to your December 28, 2023, biologics license application (BLA), submitted under section 351(a) of the Public Health Service Act for Tevimbra (tislelizumab-jsgr injection) for intravenous use.

LICENSING

We have approved your BLA for Tevimbra (tislelizumab-jsgr) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Tevimbra under your existing Department of Health and Human Services U.S. License No. 2232. Tevimbra is indicated, in combination with platinum and fluoropyrimidine-based chemotherapy, for the first-line treatment of adults with unresectable or metastatic HER2-negative gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 (≥1).

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 2°C to 8°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. 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.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on November 12, 2024, 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 761417**." 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.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

[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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4773-1 Conduct a clinical trial to further characterize the clinical effects of tislelizumab, including pharmacokinetics, activity, and safety assessments in U.S racial and ethnic minority patients with gastroesophageal cancers. The trial should enroll a sufficiently representative study population to reflect the racial and ethnic diversity of the U.S. patient population with HER2-negative, unresectable or metastatic gastroesophageal cancer and support an evaluation of comparative efficacy and safety between racial and ethnic minorities (including Black/African American and Hispanic/Latino populations) underrepresented in trial RATIONALE-305.

The timetable you submitted on December 24, 2024, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	06/2025
Final Protocol Submission:	12/2025
Trial Completion:	12/2031
Final Report Submission:	06/2032

4773-2 Conduct an appropriate analytical and clinical validation study, using clinical trial data from RATIONALE-305, to support the availability of an in vitro diagnostic device to detect PD-L1 expression that is essential for the safe and effective use of tislelizumab in patients with HER2-negative gastric/gastroesophageal junction adenocarcinoma.

The timetable you submitted on December 24, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission:	05/2026

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 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**."

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.

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:

[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

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 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** 761232 for this product, not to this BLA. **In the future, do not make submissions to this BLA**.

If you have any questions, contact Rebecca Cohen, Regulatory Health Project Manager, at (240) 402-4998.

Sincerely,

{See appended electronic signature page}

Steven Lemery, M.D., M.H.S.
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

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
01/02/2025 09:07:39 AM