CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761429Orig1s000

Trade Name: Opdivo Qvantig subcutaneous injection

Generic or Proper Name: nivolumab and hyaluronidase-nvhy

Sponsor: Bristol Myers Squibb, Company

Approval Date: December 27th, 2024

Indication: 761381 Opdivo Qvantig is indicated for:

Renal Cell Carcinoma (RCC)

- adult patients with intermediate or poor risk advanced RCC, as a first-line treatment following combination treatment with intravenous nivolumab and ipilimumab.
  Limitations of Use: OPDIVO QVANTIG is not indicated in combination with ipilimumab for the treatment of renal cell carcinoma.
- adult patients with advanced RCC, as a first-line treatment in combination with cabozantinib.
- adult patients with advanced RCC who have received prior anti-angiogenic therapy.

Melanoma

- adult patients with unresectable or metastatic melanoma.
- adult patients with unresectable or metastatic melanoma following combination treatment with intravenous nivolumab and ipilimumab.
  Limitations of Use: OPDIVO QVANTIG is not indicated in combination with ipilimumab for the treatment of unresectable or

metastatic melanoma.
- for the adjuvant treatment of adult patients with completely resected Stage IIB, Stage IIC, Stage III, or Stage IV melanoma.

Non-Small Cell Lung Cancer (NSCLC)
- adult patients with resectable (tumors ≥4 cm or node positive) NSCLC in the neoadjuvant setting, in combination with platinum-doublet chemotherapy.
- adult patients with metastatic NSCLC and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO QVANTIG.
  Limitations of Use: OPDIVO QVANTIG is not indicated in combination with ipilimumab for the treatment of metastatic NSCLC.

Squamous Cell Carcinoma of the Head and Neck (SCCHN)
- adult patients with recurrent or metastatic SCCHN with disease progression on or after a platinum-based therapy.

Urothelial Carcinoma (UC)
- adjuvant treatment of adult patients with UC who are at high risk of recurrence after undergoing radical resection of UC.
- adult patients with locally advanced or metastatic UC who:
  - have disease progression during or following platinum-containing chemotherapy.
  - have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Esophageal Cancer
- adult patients with completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease, who have received neoadjuvant chemoradiotherapy (CRT).
- adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma as first-line treatment in combination with fluoropyrimidine- and platinum-containing chemotherapy.
  Limitations of Use: OPDIVO QVANTIG is not indicated in combination with ipilimumab for the treatment of patients with unresectable advanced or metastatic ESCC.
- adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma

- adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy.

Colorectal Cancer

- adult patients with MSI-H or dMMR metastatic CRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, as monotherapy or as monotherapy following combination treatment with intravenous nivolumab and ipilimumab.
  Limitations of Use: OPDIVO QVANTIG is not indicated in combination with ipilimumab for the treatment of MSI-H or dMMR metastatic CRC.

Hepatocellular Carcinoma (HCC)

- adult patients with HCC previously treated with sorafenib and following combination treatment with intravenous nivolumab and ipilimumab.
  Limitations of Use: OPDIVO QVANTIG is not indicated in combination with ipilimumab for the treatment of HCC.

761429 Opdivo Qvantig is indicated for:

Non-Small Cell Lung Cancer (NSCLC)

- adult patients with resectable (tumors ≥4 cm or node positive) NSCLC and no known EGFR mutations or ALK rearrangements, for neoadjuvant treatment, in combination with platinum-doublet chemotherapy, followed by OPDIVO QVANTIG monotherapy as adjuvant treatment after surgery.

Urothelial Carcinoma

- adult patients with unresectable or metastatic urothelial carcinoma, as first-line treatment in combination with cisplatin and gemcitabine.

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APPROVAL LETTER

BLA 761429

BLA APPROVAL

Bristol Myers Squibb, Company
Attention: Jateh Major, PharmD
Associate Director, Global Regulatory Sciences and Policy, Oncology
P.O. Box 5326
Princeton, NJ 08543-5326

Dear Dr. Major:

Please refer to your March 29, 2024, biologics license application (BLA) and your amendments, submitted under section 351(a) of the Public Health Service Act for Opdivo Qvantig (nivolumab and hyaluronidase-nvhy) subcutaneous injection.

LICENSING

We have approved your BLA for Opdivo Qvantig (nivolumab and hyaluronidase-nvhy) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Opdivo Qvantig under your existing Department of Health and Human Services U.S. License No. 1713. This application provides for the following indications for Opdivo Qvantig subcutaneous injection:

Non-Small Cell Lung Cancer (NSCLC)

- adult patients with resectable (tumors ≥4 cm or node positive) NSCLC and no known EGFR mutations or ALK rearrangements, for neoadjuvant treatment, in combination with platinum-doublet chemotherapy, followed by OPDIVO QVANTIG monotherapy as adjuvant treatment after surgery.

Urothelial Carcinoma.

- adult patients with unresectable or metastatic urothelial carcinoma, as first-line treatment in combination with cisplatin and gemcitabine.

MANUFACTURING LOCATIONS

Under this licence, you are approved to manufacture nivolumab drug substance at Bristol-Myers Squibb Company in Devens, Massachusetts. The final formulated drug product will be manufactured and filled at (b) (4)
The final formulated nivolumab and hyaluronidase-nvhy drug product will be secondary packaged and labeled at (b) (4) You may label your product with the proprietary name, Opdivo Qvantig, and market it in 600 mg nivolumab and 10,000 units hyaluronidase per 5 mL injection in a single-dose vial.

DATING PERIOD

The dating period for Opdivo Qvantig shall be 36 months from the date of manufacture when stored at 2 - 8 °C, protected from light. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your nivolumab drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) We have approved the stability protocol in your license application for the purpose of extending the expiration dating period of your nivolumab drug substance under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Opdivo Qvantig to the Center of 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 Opdivo Quvantig, 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.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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).

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

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 enclosed carton and container labeling submitted on December 17, 2024, to BLA 761381 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 761381**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for Opdivo Qvantig was not referred to an FDA advisory committee as no significant review issues were identified during the review of this application..

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications fornew 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable due to the rarity of NSCLC and urothelial cancer in all pediatric age groups.

Refer to the pediatric PMR issued under BLA 761381 regarding your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act.

[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.

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

[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

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

ADDITIONAL COMMENTS

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 761381** for this product, not to this BLA. **In the future, do not make submissions to this BLA**.

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

Sincerely,

{See appended electronic signature page}

Steven Lemery, MD, MHS
Director
Division of Oncology 3
Office of Oncologic Disease
Office of New Drugs
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
12/27/2024 10:27:32 AM