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Section:	Prescription Drugs	**Effective Date:**	July 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	February 28, 2025
Subject:	Opdivo Qvantig	**Page:**	1 of 10

Last Review Date: June 12, 2025

Opdivo Qvantig

Description

Opdivo Qvantig (nivolumab and hyaluronidase-nvhy)

Background
Opdivo Qvantig (nivolumab and hyaluronidase-nvhy) is a monoclonal antibody formulated with an endoglycosidase to allow for subcutaneous administration. Nivolumab is a programmed death receptor-1 (PD-1) blocking antibody which is indicated to treat many categories of cancer. Nivolumab can bind to the PD-1 receptor and block its interaction with programmed death receptor ligands such as PD-L1 and PD-L2 and decrease tumor growth (1).

Regulatory Status
FDA-approved indications: Opdivo Qvantig is a combination of nivolumab, a programmed death receptor-1 (PD-1)-blocking antibody, and hyaluronidase, an endoglycosidase, indicated for the treatment of: (1)

1. Renal Cell Carcinoma (RCC)
    a. Adult patients with intermediate or poor risk advanced RCC, as a first-line treatment following combination treatment with intravenous nivolumab and ipilimumab.
        i. Limitations of Use: Opdivo Qvantig is not indicated in combination ipilimumab for the treatment of renal cell carcinoma.
    b. Adult patients with advanced RCC, as first-line treatment in combination with cabozantinib.
    c. Adult patients with advanced RCC who have received prior anti-angiogenic therapy.
2. Melanoma
    a. Adult patients with unresectable or metastatic melanoma.

b. Adult patients with unresectable or metastatic melanoma following combination treatment with intravenous nivolumab and ipilimumab.
    i. Limitations of Use: Opdivo Qvantig is not indicated in combination with ipilimumab for the treatment of unresectable or metastatic melanoma.
c. For the adjuvant treatment of adult patients with completely resected Stage IIB, Stage IIC, Stage III, or Stage IV melanoma.

3. Non-Small Cell Lung Cancer (NSCLC)
    a. Adult patients with resectable (tumors ≥4 cm or node positive) NSCLC in the neoadjuvant setting, in combination with platinum-doublet chemotherapy.
    b. 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.
    c. 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 an FDA-approved therapy for these aberrations prior to receiving Opdivo Qvantig.
        i. Limitations of Use: Opdivo Qvantig is not indicated in combination with ipilimumab for the treatment of metastatic NSCLC.
4. Squamous Cell Carcinoma of the Head and Neck (SCCHN)
    a. Adult patients with recurrent or metastatic SCCHN with disease progression on or after a platinum-based therapy.
5. Urothelial Carcinoma (UC)
    a. Adjuvant treatment of adult patients with UC who are at high risk of recurrence after undergoing radical resection of UC.
    b. Adult patients with unresectable or metastatic UC, as first-line treatment in combination with cisplatin and gemcitabine.
    c. Adult patients with locally advanced or metastatic UC who:
        i. Have disease progression during or following platinum-containing chemotherapy.
        ii. Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
6. Colorectal Cancer (CRC)
    a. Adult patients with Microsatellite instability-high (MSI-H) or mismatch repair deficient (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.

i. Limitations of Use: Opdivo Qvantig is not indicated in combination ipilimumab for the treatment of MSI-H or dMMR metastatic CRC.

7. Hepatocellular Carcinoma (HCC)
    a. Adult patients with HCC previously treated with sorafenib and following combination treatment with intravenous nivolumab and ipilimumab.
        i. Limitations of Use: Opdivo Qvantig is not indicated in combination ipilimumab for the treatment of HCC.
8. Esophageal Cancer
    a. Adult patients with completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease, who have received neoadjuvant chemoradiotherapy (CRT).
    b. Adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) as first-line treatment in combination with fluoropyrimidine- and platinum-containing chemotherapy.
        i. Limitations of Use: Opdivo Qvantig is not indicated in combination ipilimumab for the treatment of patients with unresectable advanced or metastatic ESCC.
    c. Adult patients with unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.
9. Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma
    a. Adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy.

Opdivo Qvantig carries warnings for immune-mediated adverse reactions, complications of allogeneic hematopoietic stem cell transplantation (HSCT), and embryo-fetal toxicity. Clinically significant immune-mediated adverse reactions may occur with Opdivo Qvantig therapy including pneumonitis, colitis, hepatitis, nephritis, renal dysfunction, hyperthyroidism, and hypothyroidism. Patients should be monitored for signs and symptoms of adverse reactions and based on the severity, Opdivo Qvantig should be withheld or discontinued, and corticosteroids administered. Opdivo Qvantig may cause fetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised of the potential hazard to a fetus (1).

The safety and effectiveness of Opdivo Qvantig have not been established in pediatric patients less than 18 years of age (1).

Related Policies
Bavencio, Keytruda, Loqtorzi, Opdivo, Opdualag, Tecentriq, Yervoy, Zynyz

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Opdivo Qvantig may be considered **medically necessary** if the conditions indicated below are met.

Opdivo Qvantig may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Unresectable or metastatic melanoma
   a. Used as a single agent

2. Adjuvant treatment of melanoma post resection
   a. Stage IIB, Stage IIC, Stage III, or Stage IV melanoma
   b. Used as a single agent

3. Resectable non-small cell lung cancer (NSCLC)
   a. Tumors ≥4 cm **OR** node positive
   b. Used in combination with platinum-doublet chemotherapy in the neoadjuvant setting

4. Metastatic non-small cell lung cancer (NSCLC) with **ONE** of the following:
   a. **NO** EGFR or ALK genomic tumor aberrations
      i. Disease progressed on or after platinum-based chemotherapy
      ii. Used as a single agent
   b. Positive for EGFR or ALK genomic tumor aberrations

i. Patient had disease progression on FDA approved therapy
ii. Used as a single agent

5. Advanced renal cell carcinoma with **ONE** of the following:
   a. First-line treatment in combination with cabozantinib
   b. Prior treatment with anti-angiogenic therapy
      i. Used as a single agent
   c. Patient is considered to have an intermediate or poor prognosis
      i. Used as first-line treatment following intravenous nivolumab in combination with ipilimumab
      ii. Used as a single agent

6. Recurrent or metastatic squamous cell carcinoma of the head and neck
   a. Disease must have progressed while on or after platinum-based chemotherapy
   b. Used as a single agent

7. Urothelial carcinoma with **ONE** of the following:
   a. Patient is at high risk of recurrence after undergoing radical resection
      i. Used as adjuvant treatment
      ii. Used as a single agent
   b. Unresectable or metastatic urothelial carcinoma
      i. Used as first-line treatment in combination with cisplatin and gemcitabine
   c. Locally advanced or metastatic urothelial carcinoma, used as a single agent with **ONE** of the following:
      i. Disease must have progressed while on or after platinum-based chemotherapy
      ii. Disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

8. Hepatocellular carcinoma
   a. Prior treatment with sorafenib
   b. Following treatment with intravenous nivolumab in combination with ipilimumab
   c. Used as a single agent

9. Completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease

a. Patient has received neoadjuvant chemoradiotherapy (CRT)
b. Used as a single agent

10. Unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC)
    a. Used as first-line treatment
    b. Used in combination with fluoropyrimidine- and platinum-containing chemotherapy

11. Unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC)
    a. Prior treatment with fluoropyrimidine- and platinum-based chemotherapy
    b. Used as a single agent

12. Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer
    a. Progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan
    b. Diagnosis has to be confirmed by PCR-based assay genetic testing
    c. Used as a single agent

13. Advanced or metastatic gastric cancer, gastroesophageal junction cancer, or esophageal adenocarcinoma
    a. Used in combination with fluoropyrimidine- and platinum-containing chemotherapy

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Unresectable or metastatic melanoma
   a. Used as a single agent

2. Adjuvant treatment of melanoma post resection: one renewal **only**

a. Stage IIB, Stage IIC, Stage III, or Stage IV melanoma
b. Used as a single agent

3. Resectable non-small cell lung cancer (NSCLC)
   a. Used as a single agent after surgery as adjuvant treatment
   b. **NO** known EGFR mutations or ALK rearrangements

4. Metastatic non-small cell lung cancer
   a. Used as a single agent

5. Advanced renal cell carcinoma
   a. **IF** used in combination with cabozantinib: one renewal **only**

6. Recurrent or metastatic squamous cell carcinoma of the head and neck
   a. Used as a single agent

7. Urothelial carcinoma
   a. **IF** used as adjuvant treatment in patients at high risk of recurrence after radical resection: one renewal **only**
      i. Used as a single agent
   b. **IF** used for unresectable or metastatic urothelial carcinoma, as first-line treatment in combination with cisplatin and gemcitabine: one renewal **only**

8. Hepatocellular carcinoma
   a. Used as a single agent

9. Completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease: one renewal **only**
   a. Used as a single agent

10. Unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC)
    a. Used in combination with **ONE** of the following:
       i. Fluoropyrimidine- and platinum-containing chemotherapy: one renewal **only**
       ii. Used as a single agent

11. Unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC)

a. Prior treatment with fluoropyrimidine- and platinum-based chemotherapy
b. Used as a single agent

12. Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer
    a. Used as a single agent

13. Advanced or metastatic gastric cancer, gastroesophageal junction cancer, or esophageal adenocarcinoma
    a. Used in combination with fluoropyrimidine- and platinum-containing chemotherapy: one renewal **only**

AND ALL of the following for **ALL** indications:
a. **NO** disease progression or unacceptable toxicity
b. Prescriber agrees to discontinue treatment for any immune mediated adverse reaction (encephalitis, nephritis, rash, decreased renal function and endocrinopathies) or disease progression

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Duration*

Indication	Renewal PA Duration*	Number of Renewals Allowed
Adjuvant treatment of melanoma post resection	**6** months	One renewal only
Adjuvant treatment of urothelial carcinoma (patients at high risk of recurrence after radical resection)	**6** months	One renewal only

Completely resected esophageal or gastroesophageal junction cancer with residual pathological disease	**6** months	One renewal only
Resectable non-small cell lung cancer (NSCLC) as adjuvant treatment after surgery	**12** months	One renewal only
Advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma	**18** months	One renewal only
Unresectable or metastatic urothelial carcinoma (first-line, in combination with cisplatin and gemcitabine)	**18** months	One renewal only
Esophageal squamous cell carcinoma	**18** months	Used with fluoropyrmidine- and platinum-containing chemotherapy: One renewal only
		Prior treatment with fluoropyrimidine- and platinum-based chemotherapy: Until disease progression or unacceptable toxicity
Advanced renal cell carcinoma	**18** months	Used with cabozantinib: One renewal only
		NOT being used with cabozantinib: Until disease progression or unacceptable toxicity
All other indications	**18** months	Until disease progression or unacceptable toxicity

****NO** renewal for Resectable non-small cell lung cancer (NSCLC) used as neoadjuvant treatment

Rationale

Summary
Opdivo Qvantig (nivolumab and hyaluronidase-nvhy) is a combination of a monoclonal antibody and an endoglycosidase for subcutaneous administration. Opdivo Qvantig works by binding to the programmed cell death-1 (PD-1) receptor, and blocking its interaction with PD-1 ligands, PD-L1 and PD-L2. This interaction releases the inhibitory effects of PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response, resulting in decreased tumor growth. Opdivo Qvantig carries warnings for immune-mediated adverse reactions, infusion-related reactions, complications of allogeneic HSCT and embryo-fetal toxicity. The safety and effectiveness of Opdivo Qvantig have not been established in pediatric patients less than 18 years of age (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Opdivo Qvantig while maintaining optimal therapeutic outcomes.

References

1. Opdivo Qvantig [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; December 2024.
2. NCCN Drugs & Biologics Compendium® Nivolumab and hyaluronidase-nvhy 2025. National Comprehensive Cancer Network, Inc. Accessed on April 22, 2025.

Policy History

Date	Action
February 2025	Addition to PA
June 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 12, 2025 and is effective on July 1, 2025.