Draft Revision Policy: Do Not Implement

Nivolumab and Hyaluronidase-nvhy (Opdivo Qvantig™)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

The proposal is to add text/statements in red and to delete text/statements with strikethrough:
POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Advanced Renal Cell Carcinoma

- Opdivo Qvantig, as monotherapy, is indicated for the first-line treatment of adult patients with intermediate or poor risk advanced renal cell carcinoma (RCC) following treatment with intravenous nivolumab and ipilimumab combination therapy.
- Opdivo Qvantig, in combination with cabozantinib, is indicated for the first-line treatment of adult patients with advanced RCC.
- Opdivo Qvantig, as monotherapy, is indicated for the treatment of adult patients with advanced RCC who have received prior anti-angiogenic therapy.

Unresectable or Metastatic Melanoma

- Opdivo Qvantig, as monotherapy, is indicated for the treatment of adult patients with unresectable or metastatic melanoma.
- Opdivo Qvantig, as monotherapy, is indicated for the treatment of adult patients with unresectable or metastatic melanoma following treatment with intravenous nivolumab and ipilimumab combination therapy.

Adjuvant Treatment of Melanoma
Opdivo Qvantig, as monotherapy, is indicated for the adjuvant treatment of adult patients with completely resected Stage IIB, Stage IIC, Stage III, or Stage IV melanoma.

Neoadjuvant Treatment of Resectable Non-Small Cell Lung Cancer
Opdivo Qvantig, in combination with platinum-doublet chemotherapy, is indicated as neoadjuvant treatment of adult patients with resectable (tumors ≥4 cm or node positive) non-small cell lung cancer (NSCLC).

Neoadjuvant and Adjuvant Treatment of Resectable Non-Small Cell Lung Cancer
Opdivo Qvantig, in combination with platinum-doublet chemotherapy, is indicated for the neoadjuvant treatment of adult patients with resectable (tumors ≥4 cm or node positive) NSCLC and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements, followed by Opdivo Qvantig as monotherapy in the adjuvant setting after surgical resection.
Metastatic Non-Small Cell Lung Cancer

Opdivo Qvantig, as monotherapy, is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with 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.

Squamous Cell Carcinoma of the Head and Neck
Opdivo Qvantig, as monotherapy is indicated for the treatment of adult patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

Urothelial Carcinoma

- Opdivo Qvantig, as monotherapy, is indicated for the adjuvant treatment of adult patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of UC.
- Opdivo Qvantig, in combination with cisplatin and gemcitabine, is indicated for the first-line treatment of adult patients with unresectable or metastatic UC.
- Opdivo Qvantig, as monotherapy, is indicated for the treatment of 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.

Microsatellite Instability-High or Mismatch Repair Deficient Metastatic Colorectal Cancer
Opdivo Qvantig, as monotherapy or as monotherapy following treatment with intravenous nivolumab and ipilimumab combination therapy, is indicated for the treatment of 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.

Hepatocellular Carcinoma
Opdivo Qvantig, as monotherapy, is indicated for the treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib and following treatment with intravenous nivolumab and ipilimumab.

Esophageal Carcinoma

- Opdivo Qvantig, as monotherapy, is indicated for the adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in adult patients who have received neoadjuvant chemoradiotherapy (CRT).
- Opdivo Qvantig, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).
- Opdivo Qvantig, as monotherapy, is indicated for the treatment of adult patients with unresectable advanced, recurrent or metastatic ESCC after prior fluoropyrimidine- and platinum-based chemotherapy.

Gastric Cancer, Gastroesophageal Junction Cancer, Esophageal Adenocarcinoma
Opdivo Qvantig, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the treatment of adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma.

Limitations of use:

Opdivo Qvantig is not indicated in combination with ipilimumab for the treatment of renal cell carcinoma, unresectable or metastatic melanoma, metastatic NSCLC, MSI-H or dMMR metastatic CRC, HCC, or unresectable advanced or metastatic ESCC.

Compendial Uses

Renal cell carcinoma as substitute for IV nivolumab

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- Documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.
- Documentation of EGFR mutation or ALK rearrangement status, where applicable.

EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor therapy.

COVERAGE CRITERIA

Renal Cell Carcinoma

Authorization of 6 months may be granted for treatment of renal cell carcinoma when the requested medication will be used in any of the following settings:

- As a single agent for the first-line treatment of intermediate or poor risk advanced renal cell carcinoma (RCC) following treatment with intravenous nivolumab and ipilimumab combination therapy.
- As a single agent for clear cell histology as subsequent therapy.
- As a single agent for non-clear cell histology.
- In combination with cabozantinib.

Melanoma

Authorization of 6 months may be granted for treatment of melanoma when the requested medication will be used in either of the following settings:

- As a single agent for unresectable or metastatic disease.
- As a single agent for adjuvant treatment of completely resected Stage IIB, Stage IIC, Stage III, or Stage IV disease.

Non-Small Cell Lung Cancer (NSCLC)

- Authorization of 6 months may be granted for treatment of metastatic non-small cell lung cancer when all of the following criteria are met:
  - If member has EGFR mutations or ALK rearrangements, disease has progressed on FDA-approved targeted therapy
  - The member had disease progression on or after platinum based chemotherapy.
  - The requested medication will be used as a single agent.

- Authorization of 3 months (for up to 3 cycles total) may be granted for neoadjuvant treatment of resectable non-small cell lung cancer (NSCLC) in combination with platinum based chemotherapy when there are no EGFR mutations or ALK rearrangements.
- Authorization of 6 months may be granted for neoadjuvant and adjuvant treatment of resectable non-small cell lung cancer (NSCLC) when both of the following criteria are met:
  - There are no EGFR mutations or ALK rearrangements.
  - The requested medication is used in combination with platinum based chemotherapy (for up to 4 cycles total), followed by single agent adjuvant therapy (for up to 13 cycles).

Head and Neck Cancer

Authorization of 6 months may be granted for treatment of squamous cell head and neck carcinoma when all of the following criteria are met:

- The member has recurrent or metastatic disease.
- The member had disease progression on or after platinum based chemotherapy.
- The requested medication will be used as a single agent.

Urothelial Carcinoma

- Authorization of 6 months may be granted in combination with gemcitabine and cisplatin for up to 6 cycles for first-line treatment of unresectable or metastatic urothelial carcinoma.
- Authorization of 6 months may be granted as a single agent for treatment of urothelial carcinoma when any of the following conditions are met:
  - The requested medication will be used to treat locally advanced or metastatic disease in members 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.
  - The requested medication will be used as adjuvant therapy in members who are at high risk of recurrence after undergoing radical resection.

Colorectal Cancer

Authorization of 6 months may be granted as a single agent for treatment of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer when the disease has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Hepatocellular Carcinoma

Authorization of 6 months may be granted as a single agent for treatment of hepatocellular carcinoma when member has been previously treated with sorafenib and following treatment with intravenous nivolumab and ipilimumab.

Esophageal Carcinoma

- Authorization of 6 months may be granted as a single agent for adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in members who have received neoadjuvant chemoradiotherapy (CRT).
- Authorization of 6 months may be granted as a single agent for treatment of unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

- Authorization of 6 months may be granted in combi
- nation with fluoropyrimidine- and platinum-containing chemotherapy, for first-line treatment of unresectable advanced or metastatic ESCC.

Gastric Cancer, Gastroesophageal Junction Cancer, Esophageal Adenocarcinoma

Authorization of 6 months may be granted in combination with fluoropyrimidine- and platinum-containing chemotherapy for treatment of advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma.

CONTINUATION OF THERAPY

Adjuvant Treatment of Melanoma

Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for melanoma who have not experienced disease recurrence or unacceptable toxicity.

Urothelial Carcinoma

- Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for adjuvant treatment of urothelial carcinoma who have not experienced disease recurrence or unacceptable toxicity.
- Authorization of 6 months may be granted (up to 24 months total) for continued treatment in members requesting reauthorization for first line treatment of urothelial carcinoma when the requested medication is used in combination with gemcitabine and cisplatin for up to 6 cycles followed by single agent maintenance therapy when the member has not experienced disease progression or unacceptable toxicity.

Non-Small Cell Lung Cancer

- Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for metastatic non-small cell lung cancer (NSCLC) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- Authorization of 3 months of therapy total (up to 3 cycles total) may be granted for neoadjuvant treatment of resectable NSCLC when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- Authorization of 6 months may be granted for neoadjuvant and adjuvant treatment of resectable NSCLC (up to 4 cycles in combination with chemotherapy, followed by single agent adjuvant treatment up to 13 cycles) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Renal Cell Carcinoma

Authorization of 6 months may be granted (up to 24 months total when used as a single agent) for continued treatment in members requesting reauthorization for renal cell carcinoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Esophageal Squamous Cell Carcinoma, Gastric Cancer, Gastroesophageal Junction Cancer, Esophageal Adenocarcinoma

- Authorization of 6 months may be granted (up to 24 months total) for continued treatment in members requesting reauthorization for esophageal squamous cell carcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- Authorization of 6 months may be granted (up to 24 months total) for continued treatment in members requesting reauthorization for gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. Adjuvant treatment of resected esophageal or gastroesophageal junction cancer will be limited to 12 months total therapy.

All Other Indications

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for all other indications listed in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Opdivo Qvantig (Nivolumab and Hyaluronidase- nvhy)	Colorectal Cancer	Route of Administration: Subcutaneous ≥12 year(s) ≥40kg 600/10,000mg-units every 2 weeks 900/15,000mg-units every 3 weeks 1200/20,000mg-units every 4 weeks ≥12 to <18 year(s) 30 - <40kg 300/5,000mg-units every 2 weeks 600/10,000mg-units every 4 weeks ~~600/10,000mg-units every 2 weeks~~ ~~900/15,000mg-units every 3 weeks~~ ~~1200/20,000mg-units every 4 weeks~~
Opdivo Qvantig (Nivolumab and Hyaluronidase- nvhy)	Esophageal Cancer, Gastroesophageal Junction Cancer, Gastric Cancer	Route of Administration: Subcutaneous 600/10,000mg-units every 2 weeks 900/15,000mg-units every 3 weeks 1200/20,000mg-units every 4 weeks
Opdivo Qvantig (Nivolumab and Hyaluronidase- nvhy)	Head and Neck Cancer, Squamous Cell Carcinoma	Route of Administration: Subcutaneous 600/10,000mg-units every 2 weeks 900/15,000mg-units every 3 weeks 1200/20,000mg-units every 4 weeks
Opdivo Qvantig (Nivolumab and Hyaluronidase- nvhy)	Hepatocellular carcinoma	Route of Administration: Subcutaneous 600/10,000mg-units every 2 weeks 900/15,000mg-units every 3 weeks 1200/20,000mg-units every 4 weeks
Opdivo Qvantig (Nivolumab and Hyaluronidase- nvhy)	Melanoma	Route of Administration: Subcutaneous ≥12 year(s) ≥40kg 600/10,000mg-units every 2 weeks 1200/20,000mg-units every 4 weeks

		≥12 to <18 year(s) 30 - <40kg 300/5,000mg-units every 2 weeks 600/10,000mg-units every 4 weeks ~~600/10,000mg-units every 2 weeks~~ ~~1200/20,000mg-units every 4 weeks~~
Opdivo Qvantig (Nivolumab and Hyaluronidase- nvhy)	Non-Small Cell Lung Cancer	Route of Administration: Subcutaneous 600/10,000mg-units every 2 weeks 900/15,000mg-units every 3 weeks 1200/20,000mg-units every 4 weeks
Opdivo Qvantig (Nivolumab and Hyaluronidase- nvhy)	Renal Cell Carcinoma	Route of Administration: Subcutaneous 600/10,000mg-units every 2 weeks 900/15,000mg-units every 3 weeks 1200/20,000mg-units every 4 weeks
Opdivo Qvantig (Nivolumab and Hyaluronidase- nvhy)	Urothelial Carcinoma	Route of Administration: Subcutaneous 600/10,000mg-units every 2 weeks 900/15,000mg-units every 3 weeks 1200/20,000mg-units every 4 weeks Initial: 900/15,000mg-units every 3 weeks Maintenance: 600/10,000mg-units every 2 weeks or 1200/20,000 mg-units every 4 weeks

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

REFERENCES

1. Opdivo Qvantig [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; December 2024.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed January 9, 2025.

EFFECTIVE DATE

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