CARECONTINUUM™

# UTILIZATION MANAGEMENT MEDICAL POLICY

**POLICY:** Oncology (Injectable – Programmed Death Receptor-1) – Opdivo Qvantig Utilization Management Medical Policy
- Opdivo Qvantig™ (nivolumab and hyaluronidase-nvhy subcutaneous injection – Bristol-Myers Squibb and Halozyme)

**REVIEW DATE:** 02/12/2025

## OVERVIEW

Opdivo Qvantiq, a programmed death receptor-1 (PD-1) blocking antibody and hyaluronidase-nvhy, is indicated for the following uses:[1]

- **Colorectal cancer**, in adults with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic disease that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, as monotherapy, or as monotherapy following treatment with Opdivo (nivolumab intravenous infusion) and Yervoy (ipilimumab intravenous infusion) combination therapy.
  Limitation of use: Opdivo Qvantig is not indicated in combination with Yervoy for the treatment of MSI-H or dMMR metastatic colorectal cancer.
  This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- **Esophageal cancer**:
  - In adults for adjuvant therapy for completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in patients who have received neoadjuvant chemotherapy, as monotherapy.
  - In adults for the first-line treatment of unresectable advanced or metastatic esophageal squamous cell carcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy.
    Limitation of use: Opdivo Qvantig is not indicated in combination with Yervoy for the treatment of unresectable advanced or metastatic esophageal squamous cell carcinoma.
  - In adults with unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based chemotherapy, as monotherapy.
- **Gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma**, in adults with advanced or metastatic disease in combination with fluoropyrimidine- and platinum-containing chemotherapy.
- **Head and neck squamous cell carcinoma**, in adults with recurrent or metastatic disease with progression on or after platinum-based therapy, as monotherapy.
- **Hepatocellular carcinoma**, in adults who have been previously treated with sorafenib and following treatment with Opdivo and Yervoy, as monotherapy.
  Limitation of use: Opdivo Qvantig is not indicated in combination with Yervoy for the treatment of hepatocellular carcinoma.
  This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- **Melanoma**:
  - In adults with unresectable or metastatic disease, as monotherapy.

  - In adults with unresectable or metastatic melanoma following treatment with Opdivo and Yervoy combination therapy, as monotherapy.
    Limitation of use: Opdivo Qvantig is not indicated in combination with Yervoy for the treatment of unresectable or metastatic melanoma.
  - For the adjuvant treatment of adults with completely resected Stage IIB, Stage IIC, Stage III, or Stage IV melanoma, as monotherapy.
- **Non-small cell lung cancer**:
  - In adults for the neoadjuvant treatment of resectable (tumors ≥ 4 cm or node positive) disease in combination with platinum-doublet chemotherapy.
  - In adults for the neoadjuvant treatment of resectable (tumors ≥ 4 cm or node positive) disease with no known epidermal growth factor receptor (*EGFR*) mutations or anaplastic lymphoma kinase (*ALK*) rearrangements in combination with platinum-doublet chemotherapy, followed by Opdivo Qvantig monotherapy in the adjuvant setting after surgical resection.
  - In adults with metastatic disease with disease progression on or after platinum-based chemotherapy as monotherapy. Patients with *EGFR* or *ALK* tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo Qvantig.
    Limitation of use: Opdivo Qvantig is not indicated in combination with Yervoy for the treatment of metastatic non-small cell lung cancer.
- **Renal cell carcinoma**:
  - In adults for the first-line treatment of intermediate or poor risk advanced disease following treatment with Opdivo and Yervoy combination therapy.
    Limitation of use: Opdivo Qvantig is not indicated in combination with Yervoy for the treatment of renal cell carcinoma.
  - In combination with Cabometyx® (cabozantinib tablets), for the first-line treatment of adults with advanced disease.
  - In adults with advanced disease who have received prior anti-angiogenic therapy, as monotherapy.
- **Urothelial carcinoma**:
  - For the adjuvant treatment of adult patients with urothelial carcinoma who are at high risk of recurrence after undergoing radical resection, as monotherapy.
  - In adults for the first-line treatment of unresectable or metastatic disease in combination with cisplatin and gemcitabine.
  - In adults with locally advanced or metastatic disease who have disease progression during or following platinum-containing chemotherapy, as monotherapy.
  - In adults with locally advanced or metastatic disease who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy, as monotherapy.

## Guidelines

The National Comprehensive Cancer Network (NCCN) ampullary adenocarcinoma (version 2.2025 – January 10, 2025), anal carcinoma (version 2.2025 – January 17, 2025), biliary tract cancers (version 6.2024 – January 10, 2025), bladder cancer (version 6.2024 – January 17, 2025), cervical cancer (version 2.2025 – January 31, 2025), colon cancer (version 6.2024 – January 17, 2025), gestational trophoblastic neoplasia (version 2.2025 – January 31, 2025), head and neck cancers (version 2.2025 – January 17, 2025), hepatocellular carcinoma (version 4.2024 – January 10, 2025), Kaposi sarcoma (version 2.2025 – January 14, 2025), kidney cancer (version 3.2025 – January 9, 2025), melanoma: cutaneous (version 2.2025 – January 28, 2025), Merkel cell carcinoma (version 1.2025 – January 17, 2025), mesothelioma: peritoneal (version 2.2025 – January 14, 2025), mesothelioma: pleural (version 2.2025 – January 14, 2025),

neuroendocrine and adrenal tumors (version 4.2024 – January 17, 2025), non-small cell lung cancer (version 3.2025 – January 14, 2025), rectal cancer (version 5.2024 – January 17, 2025), small bowel adenocarcinoma (version 2.2025 – January 17, 2025), small cell lung cancer (version 4.2025 – January 13, 2025), squamous cell skin cancer (version 1.2025- January 17, 2025), thyroid carcinoma (version 5.2024 – January 15, 2025), uterine neoplasms (version 2.2025 – January 31, 2025), vaginal cancer (version 4.2025 – January 31, 2025) clinical practice guidelines have addressed Opdivo Qvantig.[2-25] Each of the guidelines state that Opdivo Qvantig can be substituted for Opdivo (nivolumab intravenous infusion). However, a limitation of use is that Opdivo Qvantig is not indicated for use with Yervoy (ipilimumab intravenous infusion).

## POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Opdivo Qvantig. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Opdivo Qvantig as well as the monitoring required for adverse events and long-term efficacy, approval requires Opdivo Qvantig to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Opdivo Qvantig is recommended in those who meet one of the following criteria:

**FDA-Approved Indications**

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**1. Colon, Rectal, or Appendiceal Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):

**A)** Patient is ≥ 18 years of age; AND

**B)** Patient meets ONE of the following (i or ii):

- **i.** The tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); OR
- **ii.** The tumor is polymerase epsilon/delta (POLE/POLD1) mutation positive; AND

**C)** Patient meets ONE of the following (i, ii, or iii):

- **i.** Patient has tried chemotherapy; OR

  Note: Examples of chemotherapy are fluoropyrimidine such as fluorouracil (5-FU), and capecitabine; oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin).
- **ii.** Patient has unresectable, advanced, or metastatic disease; OR
- **iii.** The medication is used for neoadjuvant therapy; AND

**D)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND

**E)** Medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A or B):

**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR

**B)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**2. Esophageal and Esophagogastric Junction Cancer.** Approve for the duration noted if the patient meets ALL of the following (A, B, and C):

**A)** Patient is ≥ 18 years of age; AND

**B)** Approve for up to 1 year if the patient meets ONE of the following (i, ii, or iii):

**i.** Patient meets ALL of the following (a, b, and c):

**a)** Patient has completely resected esophageal or esophagogastric junction cancer with residual pathologic disease; AND

**b)** Patient received neoadjuvant chemotherapy; AND

**c)** Medication is used as monotherapy for adjuvant treatment; OR

**ii.** Approve for 1 year if the patient meets BOTH of the following (a and b):

**a)** Patient has unresectable advanced or metastatic esophageal squamous cell carcinoma; AND

**b)** Patient meets ONE of the following [(1) or (2)]:

**(1)** Medication is used first-line in combination with fluoropyrimidine- and platinum-containing chemotherapy; OR

Note: Examples of a fluoropyrimidine included fluorouracil and capecitabine. Examples of platinum agents include cisplatin and oxaliplatin.

**(2)** Medication is used as monotherapy following prior fluoropyrimidine- and platinum-containing chemotherapy; OR

Note: Examples of a fluoropyrimidine included fluorouracil and capecitabine. Examples of platinum agents include cisplatin and oxaliplatin.

**iii.** Approve for 1 year if the patient meets ALL of the following (a, b, and c):

**a)** Patient has ONE of the following [(1) or (2)]:

**(1)** Esophagogastric junction cancer; OR

**(2)** Esophageal adenocarcinoma; AND

**b)** Patient has advanced or metastatic disease; AND

**c)** Medication is used in combination with fluoropyrimidine- and platinum-containing chemotherapy; AND

Note: Examples of a fluoropyrimidine included fluorouracil and capecitabine. Examples of platinum agents include cisplatin and oxaliplatin.

**C)** Medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):

**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR

**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR

**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**3. Gastric Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

**A)** Patient is ≥ 18 years of age; AND

**B)** Patient has advanced or metastatic disease; AND

**C)** Medication will be used in combination with fluoropyrimidine- and platinum-containing chemotherapy; AND
Note: Examples of a fluoropyrimidine included fluorouracil and capecitabine. Examples of platinum agents include cisplatin and oxaliplatin.
**D)** Medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A or B):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks.

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**4. Head and Neck Squamous Cell Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient meets ONE of the following (i or ii):
**i.** Patient has non-nasopharyngeal disease; OR
**ii.** Patient meets BOTH of the following conditions (a and b):
**a)** Patient has nasopharyngeal disease; AND
**b)** Patient has recurrent, unresectable, oligometastatic, or metastatic disease; AND
**C)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
**D)** Medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A or B):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**5. Hepatocellular Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient has ONE of the following (i or ii):
**i.** Liver-confined, unresectable disease and are deemed ineligible for transplant; OR
**ii.** Extrahepatic/metastatic disease and are deemed ineligible for resection, transplant, or locoregional therapy; AND
**C)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
**D)** Medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A or B):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

**6. Melanoma.** Approve for duration noted if the patient meets ALL of the following (A, B, C, and D):
Note: This includes cutaneous melanoma and brain metastases due to melanoma.
**A)** Patient is ≥ 18 years of age; AND
**B)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
**C)** Patient meets ONE of the following (i, ii, or iii):
**i.** Approve for 1 year if the patient has unresectable, advanced, or metastatic disease; OR
**ii.** Approve for up to 3 months of treatment if Opdivo Qvantig will be used as neoadjuvant treatment; OR
**iii.** Approve for up to 1 year of treatment (total) if Opdivo Qvantig will be used as adjuvant therapy; AND
**D)** Medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A or B):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

**7. Non-Small Cell Lung Cancer.** Approve for the duration noted if the patient meets ALL of the following (A, B, and C):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient meets ONE of the following (i, ii, iii, iv, v, vi, or vii):
**i.** Approve for 1 year if the medication is used as first-line or continuation maintenance therapy and the patient meets ALL of the following (a, b, and c):
Note: This is regardless of programmed death-ligand-1 (PD-L1) status.
**a)** Patient has recurrent, advanced, or metastatic disease; AND
**b)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
**c)** The tumor is negative for actionable mutations; OR
Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (*EGFR*) mutation, anaplastic lymphoma kinase (*ALK*) fusions, *NTRK* gene fusion-positive, *ROS1, BRAF V600E, MET 14* skipping mutation, *RET* rearrangement, *NRG1*. The tumor may be *KRAS G12C* mutation positive.
**ii.** Approve for 1 year if the medication is used as first-line or subsequent therapy and the patient meets ALL of the following (a, b, and c):
Note: This is regardless of PD-L1 status.
**a)** Patient has recurrent, advanced, or metastatic disease; AND
**b)** Patient does NOT have EGFR exon 19 deletion or *L858R* mutation; *ALK*, *RET*, or *ROS1* rearrangements; AND
**c)** The tumor is positive for ONE of the following mutations [(1), (2), or (3)]:
**(1)** *BRAF V600E* mutation; OR
**(2)** *NTRK1/2/3* gene fusion; OR
**(3)** *MET* exon 14 skipping mutation; AND
**d)** The medication will NOT be used in combination with Yervoy; OR
**iii.** Approve for 1 year if the medication is used as first-line therapy and the patient meets ALL of the following (a, b, c, and d):
Note: This is regardless of PD-L1 status.

**a)** Patient has recurrent, advanced, or metastatic disease; AND
**b)** Patient does NOT have EGFR exon 19 deletion or *L858R* mutation, *ALK*, *RET*, or *ROS1* rearrangements; AND
**c)** The tumor is positive for ONE of the following mutations [(1), (2), or (3)]:
**(1)** Epidermal growth factor receptor (*EGFR*) exon 20 mutation; OR
**(2)** *ERBB2* (*HER2*) mutation; OR
**(3)** NRG1 gene fusion; AND
**d)** The medication will NOT be used in combination with Yervoy; OR

**iv.** Approve for 1 year if the medication is used as subsequent therapy and the patient meets ALL of the following (a, b, c, d, and e):
**a)** Patient has recurrent, advanced, or metastatic disease; AND
**b)** Patient does NOT have EGFR exon 19 deletion or *L858R* mutation, *ALK*, *RET*, or *ROS1* rearrangements; AND
**c)** The tumor is *EGFR S768I*, *L861Q*, and/or *G719X* mutation positive; OR
**d)** The patient has received targeted drug therapy for the specific mutation; AND
Note: Examples of targeted drug therapy include Gilotrif (afatinib tablets), Tagrisso (osimertinib tablets), erlotinib, Iressa (gefitinib tablets), Vizimpro (dacomitinib tablets).
**e)** The medication will NOT be used in combination with Yervoy; OR

**v.** Approve for 1 year if the patient meets ALL of the following (a, b, c, and d):
**a)** Patient has recurrent, advanced, or metastatic disease; AND
**b)** The medication is used as subsequent therapy; AND
**c)** The medication is used as a single agent; AND
**d)** Patient has not progressed on prior therapy with a programmed death-1 (PD-1)/PD-L1 inhibitor; AND
Note: This includes previous therapy with either one of Opdivo, Keytruda (pembrolizumab intravenous infusion), or Tecentriq (atezolizumab intravenous infusion).

**vi.** Approve for up to 4 months if the patient meets ALL of the following (a, b, and c):
**a)** Patient has resectable disease; AND
Note: Resectable disease is defined as tumors ≥ 4 cm or node positive.
**b)** The medication is used for neoadjuvant therapy; AND
**c)** The medication is used in combination with platinum-doublet chemotherapy; OR
Note: Examples of platinum-doublet chemotherapy include carboplatin plus paclitaxel, cisplatin plus pemetrexed, and cisplatin plus gemcitabine.

**vii.** Approve for 1 year (total) if the patient meets BOTH of the following (a and b):
**a)** Patient has completely resected disease; AND
**b)** Patient has received neoadjuvant treatment with Opdivo or Opdivo Qvantig; AND

**C)** Medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**8. Renal Cell Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

**A)** Patient is ≥ 18 years of age; AND
**B)** Patient has advanced, relapsed, or metastatic disease; AND
**C)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
**D)** Medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A or B):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**9. Urothelial Carcinoma**. Approve for 1 year if the patient meets BOTH of the following (A and B):
**A)** Patient is ≥ 18 years of age; AND
**B)** Medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

**Other Uses with Supportive Evidence**

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**10. Ampullary Adenocarcinoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
**A)** Patient is ≥ 18 years of age; AND
**B)** The tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
**C)** Patient meets ONE of the following (i or ii):
  **i.** The medication is used first-line for metastatic disease; OR
  **ii.** The medication is used for subsequent therapy; AND
**C)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
**E)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**11. Anal Carcinoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

**A)** Patient is ≥ 18 years of age; AND
**B)** Patient meets ONE of the following (i or ii):
  **i.** Patient meets BOTH of the following (a and b):
    **a)** Patient has locally recurrent, progressive disease; AND
    **b)** Medication is administered before proceeding to abdominoperineal resection; OR
  **ii.** Patient meets ALL of the following (a, b, and c):
    **a)** Patient has metastatic disease; AND
    **b)** Medication is used as subsequent therapy; AND
    **c)** Patient has NOT received prior immunotherapy; AND
      Note: Examples of immunotherapy include Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), Libtayo (cemiplimab intravenous infusion), and Jemperli (dostarlimab intravenous infusion).
**C)** The medication is used as a single agent; AND
**D)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**12. Biliary Tract Cancers**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient has ONE of the following (i, ii, iii, or iv):
  **i.** Unresectable disease; OR
  **ii.** Resected gross residual disease; OR
  **iii.** Metastatic disease; OR
  **iv.** The tumor is tumor mutational burden-high (TMB-H); AND
**C)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
**D)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**13. Cervical Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient has recurrent or metastatic disease; AND

**C)** Patient has programmed death ligand-1 (PD-L1) positive disease (combined positive score [CPS] ≥ 1); AND
**D)** The medication is used as second-line or subsequent therapy; AND
**E)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**14. Endometrial Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient has tried at least one prior systemic therapy; AND
Note: Examples of systemic therapy are carboplatin, paclitaxel, docetaxel, cisplatin, doxorubicin, topotecan, ifosfamide, everolimus/letrozole.
**C)** The tumor is mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H); AND
**D)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**15. Gestational Trophoblastic Neoplasia.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
**A)** Patient has multiagent chemotherapy-resistant disease; AND
Note: Examples of chemotherapy regimens contain etoposide, cisplatin/carboplatin, paclitaxel, bleomycin, ifosfamide, methotrexate.
**B)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
**C)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

**16. Kaposi Sarcoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient has relapsed or refractory disease; AND
- **B)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
- **C)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
- **A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
- **B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
- **C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

**17. Merkel Cell Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following (i, ii, or iii):
  - **i.** Patient has primary or recurrent regional disease; OR
  - **ii.** Patient has disseminated Merkel cell carcinoma; OR
  - **iii.** The medication is used as neoadjuvant therapy; AND
- **C)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
- **A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
- **B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
- **C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

**18. Mesothelioma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has ONE of the following (i, ii, iii, or iv):
  - **i.** Malignant pleural mesothelioma; OR
  - **ii.** Malignant peritoneal mesothelioma; OR
  - **iii.** Pericardial mesothelioma; OR
  - **iv.** Tunica vaginalis testis mesothelioma; AND
- **C)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
- **A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
- **B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR

**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**19. Neuroendocrine Tumors.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has advanced or metastatic disease; AND
- **C)** Patient meets ONE of the following (i or ii):
  - **i.** Patient has well differentiated, Grade 3 disease; OR
  - **ii.** Patient has poorly differentiated, large or small cell disease (other than lung); AND
- **D)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
- **E)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
- **A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
- **B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
- **C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**20. Small Bowel Adenocarcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has locally unresectable, medically inoperable, advanced, or metastatic disease; AND
- **C)** The tumor is ultra-hypermutated phenotype; AND
  Note: Ultra-hypermutated phenotype defined as tumor mutation burden > 50 mutations/megabase.
- **D)** Patients meets ONE of the following (i or ii):
  - **i.** The tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); OR
  - **ii.** The tumor is polymerase epsilon/delta (POLE/POLD1) mutation positive; AND
- **E)** The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion); AND
- **F)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
- **A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
- **B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
- **C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**21. Small Cell Lung Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND

**B)** The medication is used as second-line or subsequent therapy; AND
**C)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**22. Squamous Cell Skin Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient has locally advanced, regional, or metastatic disease; AND
**C)** According to the prescriber, the patient is not a candidate for curative surgery or curative radiation therapy; AND
**D)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**23. Thyroid Carcinoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient has metastatic disease; AND
**C)** Patient has anaplastic carcinoma; AND
**D)** The medication will be used as a single agent; AND
**E)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

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**24. Vaginal Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient has recurrent or metastatic disease; AND

**C)** Patient has programmed death ligand-1 (PD-L1) positive disease (combined positive score [CPS] ≥ 1); AND
**D)** The medication is used as second-line or subsequent therapy; AND
**E)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):
**A)** 600 mg nivolumab and 10,000 units hyaluronidase administered subcutaneously no more frequently than once every 2 weeks; OR
**B)** 900 mg nivolumab and 15,000 units hyaluronidase administered subcutaneously no more frequently than once every 3 weeks; OR
**C)** 1,200 mg nivolumab and 20,000 units hyaluronidase administered subcutaneously no more frequently than once every 4 weeks.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Opdivo Qvantig is not recommended in the following situations:

**1.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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## HISTORY

| Type of Revision | Summary of Changes | Review Date |
|---|---|---|
| New Policy | -- | 01/08/2025 |
| Early Annual Revision | **Colon, Rectal, or Appendiceal Cancer:** Added Appendiceal to Colon, Rectal, or Appendiceal cancer. The tumor is polymerase epsilon/delta mutation positive added as new option for approval. Patient has tried chemotherapy; or patient has unresectable, advanced, or metastatic disease; or medication is used for neoadjuvant therapy added as new requirement. The medication will NOT be used in combination with Yervoy (ipilimumab intravenous infusion) added as new requirement.<br>**Head and Neck Squamous Cell Carcinoma:** Added unresectable, oligometastatic to patient has recurrent, unresectable, oligometastatic, or metastatic disease. Patient has non-nasopharyngeal disease; or patient has nasopharyngeal and has recurrent, unresectable, oligometastatic, or metastatic disease added as new options for approval. The medication will NOT be used in combination with Yervoy added as new requirement.<br>**Hepatocellular Carcinoma:** Requirement patient has been previously treated with sorafenib was removed. Added liver-confined, unresectable disease and are deemed ineligible for transplant, or extrahepatic/metastatic disease and are deemed ineligible for resection, transplant, or locoregional therapy added as new options for approval. Removed requirement that the medication will be administered as monotherapy following treatment with Opdivo (nivolumab intravenous infusion) and Yervoy. Added the medication will NOT be used in combination with Yervoy as new requirement.<br>**Melanoma:** Added Note that this condition includes cutaneous melanoma and brain metastases due to melanoma. The medication will NOT be used in combination with Yervoy added as new requirement. Removed requirement that the medication is used as monotherapy. Added approve for up to 3 months of treatment if Opdivo Qvantig is used as neoadjuvant treatment as new option for approval. Removed Stage IIB, IIC, III, or IV disease from adjuvant option for approval.<br>**Non-Small Cell Lung Cancer:** Added new options for approval for first-line or continuation maintenance therapy, first-line or subsequent therapy, first-line therapy, and subsequent therapy. Added Note defining resectable disease. Removed Note defining platinum agents and Added Note with examples of platinum-doublet chemotherapy. Removed up to from approve for 1 year (total) if the patient meets BOTH of the following. Removed medication is used as monotherapy for adjuvant treatment as requirement and added patient has completely resected disease as requirement. Added Opdivo to patient has received neoadjuvant treatment with Opdivo or Opdivo Qvantig. Removed requirement that the patient is negative for epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) rearrangements. Removed option for approval that the patient has metastatic disease, has progressed on or after platinum based chemotherapy, medication will be used as monotherapy, and if the patient has EGFR | 02/12/2025 |

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|---|---|---|
| | mutations or ALK rearrangements, the patient has progressed on FDA approved therapy for these aberrations.<br>**Renal Cell Carcinoma:** Removed options for approval for intermediate or poor risk disease, advanced disease and the medication is used in combination with Cabometyx (cabozantinib tablets), and advanced disease and the patient has received prior anti-angiogenic therapy. Added requirement that the patient has advanced, relapsed, or metastatic disease. Added requirement that the medication will NOT be used in combination with Yervoy.<br>**Urothelial Carcinoma:** Removed options for approval for patient is at high-risk of recurrence after radical resection, patient has unresectable or metastatic disease, and patient has locally advanced or metastatic disease.<br>**Ampullary Adenocarcinoma:** Added new condition of approval.<br>**Anal Carcinoma:** Added new condition of approval.<br>**Biliary Tract Cancers:** Added new condition of approval.<br>**Cervical Cancer:** Added new condition of approval.<br>**Endometrial Carcinoma:** Added new condition of approval.<br>**Gestational Trophoblastic Neoplasia:** Added new condition of approval.<br>**Kaposi Sarcoma:** Added new condition of approval.<br>**Merkel Cell Carcinoma:** Added new condition of approval.<br>**Mesothelioma:** Added new condition of approval.<br>**Neuroendocrine Tumors:** Added new condition of approval.<br>**Small Bowel Adenocarcinoma:** Added new condition of approval.<br>**Small Cell Lung Cancer:** Added new condition of approval.<br>**Squamous Cell Skin Carcinoma:** Added new condition of approval.<br>**Thyroid Carcinoma:** Added new condition of approval.<br>**Vaginal Cancer:** Added new condition of approval. | |