VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – Programmed Death Receptor-1) – Opdivo Intravenous Utilization Management Medical Policy
- Opdivo® (nivolumab intravenous infusion – Bristol-Myers Squibb)

REVIEW DATE: 02/04/2026; selected revision 04/22/2026

OVERVIEW

Opdivo intravenous, a human programmed death receptor-1 (PD-1) blocking antibody, is indicated for the following uses:[1]

- **Classical Hodgkin lymphoma:**
  - For adults who have relapsed or progressed after autologous hematopoietic stem cell transplantation (auto-HSCT) and Adcetris® (brentuximab vedotin intravenous infusion) OR after three or more lines of systemic therapy that includes auto-HSCT.
  - For adult and pediatric patients ≥ 12 years of age with previously untreated Stage III or Stage IV disease in combination with doxorubicin, vinblastine, and dacarbazine (AVD).
- **Colorectal cancer**:
  - For adult and pediatric patients ≥ 12 years of age with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease in combination with Yervoy® (ipilimumab intravenous infusion).
  - For adult and pediatric patients ≥ 12 years of age with metastatic MSI-H or dMMR disease that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan.
- **Esophageal carcinoma**:
  - For adults with unresectable advanced, recurrent, or metastatic squamous cell disease after prior fluoropyrimidine- and platinum-based chemotherapy.
  - For adults with completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease, in adults who have received neoadjuvant chemoradiotherapy.
  - First-line treatment of adults with unresectable advanced or metastatic esophageal squamous cell carcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy.
  - First-line treatment of adults with unresectable advanced or metastatic esophageal squamous cell carcinoma in combination with Yervoy whose tumors express programmed death-ligand 1 (PD-L1 [≥1%]).
- **Gastric cancer, esophagogastric junction cancer, and esophageal adenocarcinoma**, for adults with advanced or metastatic disease, in combination with fluoropyrimidine- and platinum-containing chemotherapy whose tumors express PD-L1 (≥ 1%).
- **Head and neck squamous cell carcinoma**, for adults with recurrent or metastatic disease with disease progression on or after platinum-based therapy.
- **Hepatocellular carcinoma**:
  - First-line treatment of adults with unresectable or metastatic disease in combination with Yervoy.
  - For adults with unresectable or metastatic disease who have been previously treated with Nexavar® (sorafenib tablets), in combination with Yervoy.
- **Malignant pleural mesothelioma**, for adults with unresectable disease, as first-line treatment in combination with Yervoy.
- **Melanoma**, in patients ≥ 12 years of age with:
  - Unresectable or metastatic disease as a single agent.
  - Unresectable or metastatic disease in combination with Yervoy.

  - Adjuvant treatment for Stage IIB to Stage IV disease in patients who have undergone complete resection.
- **Non-small cell lung cancer**:
  - First-line treatment in combination with Yervoy, in adults with metastatic disease expressing PD-L1 (≥ 1%) as determined by an FDA-approved test, without epidermal growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations.
  - First-line treatment in combination with Yervoy and two cycles of platinum-doublet chemotherapy, in adults with recurrent or metastatic disease without *EGFR* or *ALK* genomic tumor aberrations.
  - In adults with metastatic disease 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.
  - In combination with platinum-doublet chemotherapy, as neoadjuvant treatment of adults with resectable disease (tumors ≥ 4 cm or node positive) and no known *EGFR* mutations or *ALK* rearrangements, followed by single agent Opdivo as adjuvant treatment after surgery.
- **Renal cell carcinoma**:
  - In adults with advanced disease who have received prior anti-angiogenic therapy.
  - First-line treatment in combination with Yervoy, for adults with intermediate or poor risk advanced disease.
  - First-line treatment of adults with advanced disease in combination with Cabometyx® (cabozantinib tablets).
- **Urothelial carcinoma**:
  - First-line treatment in combination with cisplatin and gemcitabine, for adults with unresectable or metastatic disease.
  - In adults with locally advanced or metastatic disease who have disease progression during or following platinum-containing chemotherapy.
  - In adults with locally advanced or metastatic disease who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
  - Adjuvant treatment of adults at high risk of recurrence after undergoing radical resection of urothelial carcinoma.

Guidelines

The use of Opdivo is recommended across multiple National Comprehensive Cancer Network (NCCN) guidelines and the NCCN Compendium.[2-40,56-58] Recommendations with a category of evidence of 2B or higher support the approval criteria outlined below.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Opdivo intravenous. 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. Because of the specialized skills required for evaluation and diagnosis of patients treated with Opdivo intravenous as well as the monitoring required for adverse events and long-term efficacy, approval requires Opdivo intravenous 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 intravenous is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. **Classic Hodgkin Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   Note: For pediatric patients, see Pediatric Hodgkin Lymphoma criteria.
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i, ii, iii, or iv):
      i. The medication is used in combination with doxorubicin, vinblastine, and dacarbazine (AVD); OR
      ii. Patient is NOT a candidate for anthracycline therapy; OR
      Note: Examples of anthracyclines include doxorubicin and daunorubicin.
      iii. Patient has had an allogeneic hematopoietic stem cell transplantation (HSCT); OR
      iv. Patient has relapsed or refractory disease; AND
   C) The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve ONE of the following dosing regimens (A or B):
   A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
   B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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2. **Colon, Rectal, or Appendiceal Cancer.** Approve for the duration noted if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 12 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 with ultra-hypermutated phenotype (tumor mutation burden > 50 mutations/megabase); AND
   C) Patient meets ONE of the following (i or ii):
      i. Approve for 1 year if the patient has unresectable, recurrent, medically inoperable, advanced, or metastatic disease; OR
      ii. Approve for 6 months if the medication is used for neoadjuvant therapy; AND
   D) The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve ONE of the following dosing regimens (A, B, C, or D):
   A) 240 mg administered as an intravenous infusion not more frequently than once every 2 weeks; OR
   B) 480 mg administered as an intravenous infusion not more frequently than once every 4 weeks; OR
   C) 3 mg/kg administered as an intravenous infusion not more frequently than once every 2 weeks; OR
   D) 6 mg/kg administered as an intravenous infusion not more frequently than once every 4 weeks.

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3. **Esophageal and Esophagogastric Junction 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 received preoperative chemotherapy and the patient has residual disease; OR

Note: Examples of chemotherapy include 5-fluorouracil plus either cisplatin or oxaliplatin; and paclitaxel plus carboplatin.

ii. Patient meets ALL of the following (a, b, and c):
- **a)** Patient has adenocarcinoma; AND
- **b)** The tumor is microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR); AND
- **c)** The medication is used as neoadjuvant or perioperative immunotherapy; OR

iii. Patient meets BOTH of the following (a and b):
- **a)** Patient meets ONE of the following [(1), (2), or (3)]:
  - **(1)** Patient is not a surgical candidate; OR
  - **(2)** Patient has unresectable locally advanced, recurrent, or metastatic disease; OR
  - **(3)** The medication is used as induction therapy in patients planned for esophagectomy; AND
- **b)** Patient meets ONE of the following [(1), (2), or (3)]:
  - **(1)** Patient has squamous cell carcinoma; OR
  - **(2)** Patient has adenocarcinoma and the disease is human epidermal growth factor receptor 2 (HER2) negative; OR
  - **(3)** The tumor is MSI-H or dMMR; AND

C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A, B, C, or D):
A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 360 mg as an intravenous infusion administered not more frequently than once every 3 weeks; OR
C) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
D) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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4. Gastric 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) 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.** Patient meets BOTH of the following (a and b):
  - **a)** Patient has human epidermal growth factor receptor 2(HER2) overexpression negative disease; AND
  - **b)** The tumor expression for programmed death-ligand 1 (PD-L1) has a combined positive score (CPS) ≥ 1; AND

C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A, B, C, or D):
A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 360 mg as an intravenous infusion administered not more frequently than once every 3 weeks; OR
C) 1 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks; OR
D) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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5. Head and Neck Squamous 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 non-nasopharyngeal disease; OR
ii. Patient has mucosal melanoma; OR
iii. 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 is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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6. Hepatocellular 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 or ii):
i. The medication is being used as first line and according to the prescriber, the patient has ONE of the following (a or b):
a) Liver-confined, unresectable disease and is deemed ineligible for transplant; OR
b) Extrahepatic/metastatic disease and is deemed ineligible for resection, transplant, or locoregional therapy; OR
ii. The medication is being used for 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) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
C) 1 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

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7. Melanoma. Approve for the duration noted if the patient meets ALL of the following (A, B, and C):
Note: This includes cutaneous melanoma, brain metastases due to melanoma, and uveal melanoma.
A) Patient is ≥ 12 years of age; AND
B) Patient meets ONE of the following (i, ii, or iii):
i. Approve for 1 year if the patient has unresectable, advanced, or metastatic melanoma; OR
ii. Approve for up to 3 months if the medication will be used as neoadjuvant treatment; OR
iii. Approve for up to 1 year (total) if the medication will be used as adjuvant treatment; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A, B, C, D, or E):
A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
C) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
D) 1 mg/kg as an intravenous infusion not more frequently than once every 3 weeks; OR
E) 6 mg/kg as an intravenous infusion not more frequently than once every 4 weeks.

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8. Mesothelioma. 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 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 is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 360 mg as an intravenous infusion administered not more frequently than once every 3 weeks; OR
B) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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9. Non-Small Cell Lung Cancer – Neoadjuvant and Adjuvant. 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) The tumor is negative for the following actionable biomarkers: epidermal growth factor receptor (*EGFR*) *exon 19 deletion* or *exon 21 L858R*, anaplastic lymphoma kinase (*ALK), RET,* or *ROS1*; AND
C) Patient has Stage IB to Stage III disease and meets ONE of the following (i or ii):
i. The medication is used as neoadjuvant therapy in combination with platinum chemotherapy; OR
Note: Examples of platinum chemotherapy agents include cisplatin and carboplatin.
ii. The medication is used as adjuvant therapy and meets BOTH of the following (a and b):
a) The medication is used as a single-agent; AND
b) Patient has received neoadjuvant treatment with Opdivo or Opdivo Qvantig (nivolumab and hyaluronidase-nvhy subcutaneous injection); AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 360 mg as an intravenous infusion administered not more frequently than once every 3 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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10. Non-Small Cell Lung Cancer – Recurrent, Advanced, or Metastatic Disease. 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 tumor is negative for the following actionable biomarkers: epidermal growth factor receptor *(EGFR) exon 19 deletion* or *exon 21 L858R*, anaplastic lymphoma kinase *(ALK), RET,* and *ROS1*; AND
C) Patient meets ONE of the following (i, ii, iii, iv, or v):
i. Patient meets BOTH of the following (a and b):
a) The medication is used as first-line therapy in combination with Yervoy (ipilimumab intravenous infusion); AND
b) The tumor is positive for ONE of the following [(1), (2), or (3)]:
(1) Epidermal growth factor receptor (*EGFR*) exon 20 mutation; OR
(2) *ERBB2* (*HER2*) mutation; OR
(3) *NRG1* gene fusion; OR
ii. Patient meets BOTH of the following (a and b):
a) The medication is used as first-line or subsequent therapy in combination with Yervoy; AND
b) The tumor is positive for ONE of the following [(1), (2), or (3)]:

(1) *BRAF V600E* mutation; OR
(2) *NTRK1/2/3* gene fusion; OR
(3) *MET* exon 14 skipping mutation; OR

iii. Patient meets BOTH of the following (a and b):
a) The medication is used as subsequent therapy in combination with Yervoy; AND
b) The tumor is *EGFR S768I*, *L861Q*, and/or *G719X* mutation positive; OR

iv. Patient meets ALL of the following (a, b, and c):
a) The medication is used as subsequent therapy; AND
b) The medication is used as a single agent; AND
c) Patient has not progressed on prior therapy with a programmed death-1 (PD-1)/programmed death ligand 1 (PD-L1) inhibitor; OR
Note: This includes previous therapy with either one of Opdivo intravenous, Keytruda (pembrolizumab intravenous infusion), or Tecentriq (atezolizumab intravenous infusion).

v. Patient meets ALL of the following (a and b):
a) The medication is used as first-line or continuation maintenance therapy in combination with Yervoy; AND
b) The tumor has no actionable mutations; AND
Note: The tumor does NOT have the following mutations: *EGFR exon 19* deletion*, EGFR exon 21 L858R, EGFR S768I, EGFR L861Q, EGFR G719X, EGFR exon 20* insertion*, ALK* rearrangement, *ROS1* rearrangement*, BRAF V600E, NTRK 1/2/3* gene fusion*, METex14* skipping*, RET* rearrangement, *ERBB2 (HER2), and NRG1* gene fusion.

D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A, B, C, or D):
A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 360 mg as an intravenous infusion administered not more frequently than once every 3 weeks; OR
C) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
D) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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11. Pediatric Hodgkin Lymphoma. 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 or ii):
i. Patient meets ALL of the following (a, b, c, and d):
a) Patient is ≥ 12 years of age and < 18 years of age; AND
b) Patient has Stage III-IV disease; AND
c) The patient has untreated disease; AND
d) The medication is used in combination with doxorubicin, vinblastine, and dacarbazine (AVD); OR
ii. Patient has relapsed or refractory disease; 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) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
C) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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12. Renal 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 has ONE of the following (i, ii, or iii):
  i. Stage IV disease; OR
  ii. Relapsed disease; OR
  iii. Hereditary leiomyomatosis and renal cell cancer; 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) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
C) 3 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

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13. 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) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A, B, or C):
A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
C) 360 mg as an intravenous infusion administered not more frequently than once every 3 weeks.

Other Uses with Supportive Evidence

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14. Ampullary Adenocarcinoma. 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 tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); 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) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
C) 3 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

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15. 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 has locally recurrent, metastatic, or progressive disease; AND
C) Patient meets ONE of the following (i or ii):
  i. The medication is administered before proceeding to abdominoperineal resection; OR
  ii. The medication is used as subsequent 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) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
C) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

16. Biliary Tract Cancers. 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 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 is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A, B, or C):
- **A)** 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- **B)** 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
- **C)** 1 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

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17. Bone 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 ONE of the following conditions (i, ii, iii, iv, or v):
  - **i.** Chondrosarcoma; OR
  - **ii.** Chordoma; OR
  - **iii.** Ewing sarcoma; OR
  - **iv.** Osteosarcoma; OR
  - **v.** High-grade undifferentiated pleomorphic sarcoma; AND
- **C)** Patient has unresectable or metastatic disease; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks.

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18. Cervical 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 recurrent or metastatic disease; AND
- **C)** The medication is used as subsequent therapy; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks.

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19. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. 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 has histologic Richter transformation; AND
- **C)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 200 mg administered by intravenous infusion no more frequently than once every 3 weeks.

20. 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 recurrent or metastatic disease; AND
- **C)** Patient meets ONE of the following (i or ii):
  - **i.** Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors; OR
  - **ii.** Patient has tumor mutation burden-high (TMB-H) tumors; 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)** 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- **B)** 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
- **C)** 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

21. Extranodal NK/T-Cell Lymphomas. 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 has received an asparaginase-based chemotherapy regimen; AND
  Note: Examples of asparaginase-based chemotherapy are dexamethasone, ifosfamide, pegaspargase, etoposide; and gemcitabine, pegaspargase, oxaliplatin.
- **C)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
- **A)** 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- **B)** 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

22. Gestational Trophoblastic Neoplasia. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient has multiagent chemotherapy-resistant disease; AND
  Note: Examples of chemotherapy regimens contain etoposide, cisplatin/carboplatin, paclitaxel, bleomycin, ifosfamide, methotrexate.
- **B)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
- **A)** 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- **B)** 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

23. Kaposi Sarcoma. 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 has relapsed or refractory disease; AND
- **C)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
- **A)** 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- **B)** 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

24. 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, iii, or vi):
  i. Patient meets BOTH of the following (a and b):
    a) Patient has primary or recurrent regional disease; AND
    b) According to the prescriber, curative surgery and curative radiation therapy are not feasible; OR
  ii. Patient has metastatic (disseminated) disease; OR
  iii. Patient has in-transit regional disease; OR
  iv. 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 or B):
A) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks.

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25. 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 locoregional unresectable, advanced, or metastatic disease; AND
C) Patient meets ONE of the following (i, ii, iii, iv, or v):
  i. Patient has well differentiated, Grade 3 disease; OR
  ii. Patient has extrapulmonary poorly differentiated neuroendocrine carcinoma; OR
  iii. Patient has large or small cell disease; OR
  iv. Patient has mixed neuroendocrine-non-neuroendocrine neoplasm; OR
  v. Patient has adrenocortical carcinoma; AND
D) The medication is used in combination with Yervoy (ipilimumab intravenous infusion); AND
E) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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26. Pancreatic Cancer. 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 ONE of the following (i, ii, or iii):
  i. Locally advanced disease; OR
  ii. Metastatic disease; OR
  iii. Recurrent disease; AND
C) The tumor is tumor mutational burden-high (TMB-H); AND
D) The medication is used as subsequent therapy; AND
E) The medication is 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 or B):
A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

27. Pediatric Diffuse High-Grade Gliomas. 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 hypermutant tumor diffuse high-grade glioma; AND
- **C)** Patient meets ONE of the following (i or ii):
  - **i.** The medication is used for adjuvant treatment; OR
  - **ii.** The medication is used for recurrent or progressive disease; 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)** 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- **B)** 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
- **C)** 3 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

28. Primary Mediastinal Large B-Cell Lymphoma. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient has relapsed or refractory disease; AND
- **B)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
- **A)** 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- **B)** 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

29. Small Bowel Adenocarcinoma. 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 unresectable, medically inoperable, advanced, or metastatic disease; AND
- **C)** 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 with ultra-hypermutated phenotype (tumor mutation burden > 50 mutations/megabase); 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)** 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- **B)** 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
- **C)** 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

30. 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 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) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
C) 1 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

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31. Soft Tissue Sarcoma. 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 has ONE of the following (i or ii):
i. Patient has advanced, unresectable, progressive, or metastatic disease and has ONE of the following (a, b, c, d, e, f, or g):
a) Myxofibrosarcoma; OR
b) Undifferentiated pleomorphic sarcoma; OR
c) Dedifferentiated liposarcoma; OR
d) Cutaneous angiosarcoma; OR
e) Undifferentiated sarcoma; OR
f) Rhabdomyosarcoma; OR
g) Tumor mutation burden-high (TMB-H); OR
ii. Angiosarcoma; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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32. 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 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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33. Thyroid 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 metastatic disease; AND
C) Patient has anaplastic carcinoma; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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34. Vaginal 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 recurrent or metastatic disease; AND
C) The medication is used as subsequent therapy; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks.

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35. Vulvar 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, recurrent, or metastatic disease; AND
C) The medication is used as subsequent therapy; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Opdivo intravenous 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
Annual Revision	**Classic Hodgkin Lymphoma:** Removed "patient is not eligible for transplant" as an option for approval. **Colon, Rectal, or Appendiceal Cancer:** Added the tumor is polymerase epsilon/delta (POLE/POLD1) mutation positive as a new option for approval. **Esophageal and Esophagogastric Junction Carcinoma:** For option of approval Bii, removed requirement that patient has tried chemotherapy. For option of approval Biv, removed requirement that the patient has squamous cell carcinoma, that the tumor is negative for human epidermal growth factor receptor 2 overexpression, and the medication will be used for first-line therapy. Added requirement that the tumor is microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR). Revised fluoropyrimidine and platinum containing chemotherapy to fluoropyrimidine and oxaliplatin containing chemotherapy. Added additional option of approval for patient with adenocarcinoma, tumor is MSI-H or dMMR, and the medication is used for neoadjuvant or perioperative therapy. **Gastric Cancer:** Added option of approval for patient with locoregional disease, tumor is MSI-H or dMMR, and medication is used as neoadjuvant or perioperative therapy. Added option of approval for patient with unresectable locally advanced, recurrent, or metastatic disease, OR patient is not a surgical candidate, tumor is MSI-H or dMMR, and the medication will be used in combination with Yervoy (ipilimumab intravenous infusion) or with a fluoropyrimidine and oxaliplatin. Removed requirement that the tumor expression for programmed death-ligand 1 has a combined score ≥ 5. **Hepatocellular Carcinoma:** Removed "including hepatobiliary cancers" from the condition of approval. Added requirement that the patient has ONE of the following: unresectable disease and is not a transplant candidate; liver-confined disease, inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease; OR metastatic disease or extensive liver tumor burden. Added requirement that if the medication is used for first-line therapy, the patient has Child-Pugh Class B liver disease and the medication is used as a single agent. **Melanoma:** Added 1 mg/kg as an intravenous (IV) infusion no more frequently than once every 3 weeks and 6 mg/kg as an IV infusion no more frequently than once every 4 weeks as additional dosing regimens. Removed Note from adjuvant treatment criterion. **Mesothelioma:** Removed patient has unresectable disease as a requirement for the first-line use of Opdivo. **Non-Small Cell Lung Cancer:** Added the following to the Note for first-line or continuation maintenance therapy: *KRAS G12C* is not considered an actionable mutation (the tumor may be *KRAS G12C* mutation positive). Revised Bii: Opdivo is used as first-line therapy and the patient meets ALL of the following to Opdivo is used as first-line or subsequent therapy and the patient meets ALL of the following. Revised Biii: Opdivo is used as first-line or subsequent therapy to Opdivo is used as first-line therapy; and removed *KRAS G12C* from list of mutations. **Biliary Tract Cancers:** Added new condition of approval. **Cervical Cancer:** Added requirement that the patient has recurrent or metastatic disease. **Gestational Trophoblastic Neoplasia:** Removed patient has tried at least one previous chemotherapy regimen for recurrent or progressive disease and patient has methotrexate resistant high-risk disease as options for approval. Added requirement that the patient has multiagent chemotherapy-resistant disease. **Small Cell Lung Cancer:** Added 1 mg/kg as an IV infusion not more frequently than once every 3 weeks and 3 mg/kg as an IV infusion not more frequently than once every 2 weeks as additional dosing regimens. Remove 480 mg as an IV infusion not more frequently than once every 4 weeks as a recommended dosing regimen. **Soft Tissue Sarcoma:** Added new condition of approval.	01/31/2024
Selected Revision	**Urothelial Carcinoma:** The requirement that the patient has tried at least one other chemotherapy regimen or the patient is at high risk of recurrence after radical resection of the tumor has been removed.	03/20/2024
Annual Revision	**Classical Hodgkin Lymphoma:** Requirement that the patient has tried three or more systemic regimens and this includes an auto-hematopoietic stem cell transplant as one line of therapy was removed. Added new option for approval if the medication is used as primary treatment, in combination with AVD (doxorubicin, vinblastine, dacarbazine),	02/12/2025

	or Adcetris (brentuximab intravenous infusion), or as a single agent. Allogeneic was added as descriptor to patient has had an allogeneic hematopoietic stem cell transplant. As a single agent added to patient has relapsed or refractory disease and the medication is used as a single agent, or in combination with Adcetris or ICE (ifosfamide, carboplatin, and etoposide). **Esophageal and Esophagogastric Junction Carcinoma:** Added medication is used as induction therapy in patients planned for esophagectomy as new option for approval. The tumor expression for programmed death ligand-1 (PD-L1) has a combined positive score (CPS) ≥ 5 was removed. **Gastric Cancer:** 1 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks and 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks were added as additional dosing regimens. **Head and Neck Squamous Cell Carcinoma:** Opdivo is used in combination with cisplatin and gemcitabine removed as an option for approval. **Hepatocellular Carcinoma:** If the medication is used first-line, the patient has Child-Pugh Class B liver disease, and the medication is used as a single agent was removed as an option for approval. Liver-confined disease, inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease removed as an option for approval. Added liver-confined and are deemed ineligible for, and removed candidate from liver confined, unresectable disease and are deemed ineligible for transplant. Added extrahepatic and are deemed ineligible for resection, transplant, or locoregional therapy, and removed extensive liver tumor burden from extrahepatic/metastatic disease and are deemed ineligible for resection, transplant, or locoregional therapy. **Melanoma:** Added approve for up to 3 months of treatment if Opdivo will be used as neoadjuvant treatment as new option for approval. **Non-Small Cell Lung Cancer:** Approval duration changed from 1 year to the duration noted. Added approve for 1 year for first-line or continuation therapy, first-line or subsequent therapy, first-line therapy, and subsequent therapy. Removed criteria that Opdivo will be used in combination with Yervoy. Added *NRG1* and removed *KRAS G12C* is not considered an actionable mutation from the Note. Added patient does not have EGFR exon 19 deletion or *L858R* mutation; *ALK*, *RET*, or *ROS1* rearrangements as a new requirement for first-line therapy, first-line or subsequent therapy, and subsequent therapy. Removed *RET* rearrangement from the list of mutations for first-line or subsequent therapy. Added *NRG1* gene fusion to list of mutations for first-line therapy. Removed EGFR exon 19 deletion or exon 21 *L858R*, Anaplastic lymphoma kinase (*ALK*) rearrangement, and *ROS1* rearrangement from list of mutations for subsequent therapy. Removed Xalkori, Rozlytrek, and Zykadia from the Note. Removed patient has tried systemic chemotherapy, and the corresponding Note as a requirement. Added the medication is used as subsequent therapy. Added the medication is used as a single agent as a requirement. Removed if the tumor is positive for an actionable mutation, the patient has received targeted drug therapy for the specific mutation and the corresponding Note. Added approve for 4 months for neoadjuvant therapy. Added approve for 1 year if the patient has completed resected disease and the patient has received neoadjuvant treatment with Opdivo as new option for approval. **Ampullary Adenocarcinoma:** Removed unresectable localized disease, Stage IV resected disease, and metastatic disease at initial presentation as options for approval. Added metastatic disease to the medication is used first-line for metastatic disease. **Anal Carcinoma:** Removed patient has tried at least one chemotherapy regimen and the corresponding Note as a requirement. Added patient has locally recurrent, progressive disease and medication is administered before proceeding to abdominoperineal resection as new option for approval. Added patient has metastatic disease, medication is used as subsequent therapy, and patient has not received prior immunotherapy as new option for approval. Added medication is used as a single agent as new requirement. **Biliary Tract Cancers:** The tumor is tumor mutation burden-high was moved from a requirement to an option for approval. Removed requirement that the medication is used in combination with Yervoy. **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:** Added new condition of approval. **Kaposi Sarcoma:** Removed patient has classic disease as a requirement. Added single agent to the medication is used as a single agent or in combination with Yervoy. Added 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks as new dosing regimen.	

	Merkel Cell Carcinoma: Added patient has primary or recurrent regional disease as new option of approval. **Pancreatic Cancer:** Added new condition of approval. **Pediatric Hodgkin Lymphoma:** Added patient is ≥ 12 and < 18 years of age, patient has intermediate or high risk disease, medication is used for primary treatment, and in combination with doxorubicin, vinblastine, and dacarbazine as a new option for approval. **Small Bowel Adenocarcinoma:** Added locally unresectable, medically inoperable to patient has locally unresectable, medically inoperable, advanced, or metastatic disease. Added the tumor is ultra-hypermutated phenotype as new requirement. Added the tumor is polymerase epsilon/delta mutation positive as new option for approval. **Squamous Cell Skin Cancer:** Added new condition of approval. **Thyroid Cancer:** Added new condition of approval. **Vaginal Cancer:** Added new condition of approval.	
Selected Revision	**Melanoma:** Revised patient age from ≥ 18 years to ≥ 12 years of age.	03/26/2025
Selected Revision	**Non-Small Cell Lung Cancer:** The note was updated to remove "The tumor may be *KRAS G12C* mutation positive." **Colon, Rectal, or Appendiceal Cancer:** Added 6 mg/kg as an intravenous infusion administered not more frequently than once every 4 weeks as a dosing option. **Urothelial Carcinoma:** Added 360 mg as an intravenous infusion administered not more frequently than once every 3 weeks as a dosing option	04/30/2025
Early Annual Revision	**Colon, Rectal, or Appendiceal Cancer:** The requirement that the tumor is polymerase epsilon/delta (POLE/POLD1) mutation was changed to also require ultra-hypermutated phenotype (tumor mutation burden > 50 mutations/megabase). The requirement that the patient has unresectable, advanced, or metastatic disease was changed to also include medically inoperable. **Esophageal and Esophagogastric Junction Cancer:** The requirement that the tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 1 was added under patient has adenocarcinoma. **Gastric Cancer:** The requirement of unresectable locoregional disease was added to the patient has locally advanced, recurrent, or metastatic disease. Also, the tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 1 was added as an option for approval. **Head and Neck Squamous Cell Carcinoma:** Mucosal melanoma was added as an option for approval. **Hepatocellular Carcinoma:** The medication is used for first-line and for subsequent therapy were added as options for approval. **Non-Small Cell Lung Cancer – Neoadjuvant and Adjuvant:** The condition of approval was changed to as listed. Previously, all non-small cell lung cancer (NSCLC) was addressed more generally under NSCLC. A requirement was added that the tumor is negative for the following actionable biomarkers: epidermal growth factor receptor *(EGRF) exon 19 deletion* or *exon 21 L858R, anaplastic lymphoma kinase (ALK), RET, and ROS1*. The requirement that the patient has resectable disease, has been changed to patient has Stage II or Stage III disease. The medication is used as single-agent adjuvant therapy was added as an approval option. The approval duration was changed to 1 year for both adjuvant and neoadjuvant treatment therapy. **Non-Small Cell Lung Cancer – Recurrent, Advanced, or Metastatic Disease:** Indication was changed to as listed. Previously, all non-small cell lung cancer (NSCLC) was addressed more generally under NSCLC. Added a requirement that the tumor is negative for the following actionable biomarkers: epidermal growth factor receptor *(EGRF) exon 19 deletion* or *exon 21 L858R, anaplastic lymphoma kinase (ALK), RET, and ROS1*. For first-line therapy, added in combination with Yervoy (ipilimumab intravenous infusion) as an approval option. For first-line or subsequent therapy, added in combination with Yervoy. For subsequent therapy, added in combination with Yervoy and the patient has received targeted drug therapy for the specific mutation was removed as an approval option. For use as first-line or continuation maintenance therapy; changed the requirement that "the tumor is negative for actionable mutations" to "the tumor has no actionable mutations; a Note was added to clarify that the tumor does not have the following mutations: *EFGR exon 19* deletion, *EFGR exon 21 L858R, EFGR S768I, EGFR L861Q, EGFR G719X, EGFR exon 20* insertion, *ALK* rearrangement, *ROS1* rearrangement, *BRAF V600E, NTRK 1/2/3* gene fusion, *METex14* skipping, *RET* rearrangement, *ERBB2 (HER2),* and *NRG1* gene fusion. Additionally, in combination	08/06/2025

	with Yervoy was added to the medication is used as first-line or continuation maintenance therapy. **Renal Cell Carcinoma:** The requirement that the patient has advanced, relapsed, or metastatic disease was changed to be Stage IV, relapsed, or hereditary leiomyomatosis disease and renal cell cancer. **Anal Carcinoma:** The approval option "patient has not received prior immunotherapy" was modified to "patient has not received prior checkpoint inhibitors." The Note was modified to add Zynyx (retifanlimab-dlwr intravenous infusion), Loqtorzi (toripalimab-tpzi intravenous infusion), Tevimbra (tislelizumab-jsgr intravenous infusion) to the examples. **Bone Cancer:** Patient has no satisfactory alternative treatment options has been removed as an approval requirement. **Endometrial Carcinoma:** The requirements that the patients has recurrent or metastatic disease and the medication will be used as a single-agent were added. The patient has tried at least one prior systemic therapy was removed as an approval requirement. **Kaposi Sarcoma:** The requirement that the patient is ≥ 18 years of age was added. **Merkel Cell Carcinoma:** Patient has primary or recurrent locally advanced disease, and according to the prescriber curative surgery and curative radiation therapy are not feasible was added as an approval option. For regional disease a requirement that and according to the prescriber, curative surgery and curative radiation therapy are not feasible" was added. The requirement the patient has disseminated Merkel cell carcinoma was changed to the patient has metastatic (disseminated) disease. **Neuroendocrine Tumors:** Locoregional unresectable disease was added as an approval option. The following were added as options of approval: extrapulmonary poorly differentiated neuroendocrine carcinoma; large or small cell disease; mixed neuroendocrine-non-neuroendocrine neoplasm; and adrenocortical carcinoma. Poorly differentiated, large or small cell disease (other than lung) was removed as an approval option. **Pediatric Hodgkin Lymphoma:** Patient has intermediate or high risk disease was changed to the patient has Stage III-IV disease. The patient has relapsed or refractory disease was added as an approval option. The patient meets ONE of the following: the medication is used as single-agent or the medication is used in combination with ifosfamide, carboplatin, and etoposide (ICE) was added as approval options. Additionally, if used for re-induction therapy was changed to the medication is used for re-induction therapy. **Primary Mediastinal Large B-Cell Lymphoma:** The qualifier "after a partial response to therapy for relapsed or refractory disease" was removed from the medication is used in combination with Adcetris (brentuximab intravenous infusion). **Small Bowel Adenocarcinoma:** Patient has locally unresectable, medically inoperable, advanced , or metastatic disease was changed to the patient meets ONE of the following: patient has locally unresectable or medically inoperable disease; patient has advanced or metastatic disease and has not received prior checkpoint inhibitors. The requirement that the tumor is ultra hypermutated phenotype was moved to apply only to a tumor that is polymerase epsilon/delta (POLE/POLD1) mutation positive. Tumor mutation burden > 50 mutations/megabase was added as a descriptor of ultra-hypermutated phenotype. **Soft Tissue Sarcoma:** Unresectable or progressive has been added to the patient has advanced or metastatic disease. Rhabdomyosarcoma was added as an approval option. **Vulvar Cancer:** A requirement that the medication is used as subsequent therapy was added. The patient has tried at least one prior systemic therapy was removed.	
Early Annual Revision	The policy name was changed from "Oncology (Injectable – Programmed Death Receptor-1) – Opdivo" to "Oncology (Injectable – Programmed Death Receptor-1) – Opdivo Intravenous". Throughout the policy, wording was changed from Opdivo to Opdivo intravenous. **Classic Hodgkins Lymphoma:** When the medication is used as primary treatment, the options of approval that the medication is used in combination with AVD and the corresponding Note; the medication is used in combination with Adcetris (brentuximab intravenous infusion); and the medication is used as a single agent were removed. The option for approval that the patient has relapsed or refractory disease and the medication is used as a single agent or in combination with Adcetris or ICE (ifosfamide, carboplatin, and etoposide) was modified to the patient has relapsed or refractory disease. **Colon, Rectal, or Appendiceal Cancer:** The approval duration was modified from approve for 1 year to approve for the duration noted. The option of approval that the	02/04/2026

	patient has tried chemotherapy and the corresponding Note was removed. The option of approval that the patient has unresectable, medically inoperable, advanced, or metastatic disease was modified to approve for 1 year if the patient has unresectable, recurrent, medically inoperable, advanced, or metastatic disease. The approval option that the medication is used for neoadjuvant therapy was modified to approve for 6 months if the medication is used for neoadjuvant therapy. **Esophageal and Esophagogastric Junction Carcinoma:** The option of approval that according to the prescriber, the patient has residual disease was modified to the patient has residual disease. The option of approval that according to the prescriber, the patient is not a surgical candidate was modified to the patient is not a surgical candidate. When the patient has adenocarcinoma and the disease is human epidermal growth factor receptor 2 (HER2) negative, the options of approval that the tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 1; AND the medication is used in combination with fluoropyrimidine and oxaliplatin were removed along with the corresponding Note. When the tumor is MSI-H or dMMR, the options for approval that the medication will be used in combination with one of the following: Fluoropyrimidine and oxaliplatin containing chemotherapy; OR Yervoy (ipilimumab intravenous infusion) and the corresponding Note were removed. **Gastric Cancer:** The options for approval that the patient has locoregional disease and the medication is used as neoadjuvant or perioperative immunotherapy was removed. The options for approval that the patient has unresectable locally advanced, unresectable locoregional, recurrent, or metastatic disease and the according to the prescriber, the patient is not a surgical candidate were removed. The option of approval that the disease is negative for HER2 overexpression was modified to the patient has human epidermal growth factor receptor 2(HER2) over expression. The option of approval that the tumor expression for PD-L1 as determined by an approved test has a CPS ≥ 1 was modified to the tumor expression for PD-L1 has a CPS ≥ 1. The approval options that the patient has unresectable locally advanced, unresectable locoregional, recurrent, or metastatic disease and according to the prescriber, the patient is not a surgical candidate was removed when the patient has HER2 overexpression negative disease. When the tumor is MSI-H or dMMR, the options for approval that the medication will be used in combination with one of the following: Fluoropyrimidine and oxaliplatin containing chemotherapy; OR Yervoy and the corresponding Note were removed. **Mesothelioma:** The requirement that if used as first-line therapy, the medication is used in combination with Yervoy was removed. **Non-Small Cell Lung Cancer – Neoadjuvant and Adjuvant:** The requirement that the patient has Stage II or Stage III disease was modified to the patient has Stage IB or Stage III disease. **Ampullary Adenocarcinoma:** The requirement that the patient meets ONE of the following: the medication is used as first-line for metastatic disease or the medication is used for subsequent therapy was removed. The requirement that the medication is used in combination with Yervoy was removed. **Anal Carcinoma:** The option that the patient has not received prior check point inhibitors and the corresponding Note was removed. The requirement that the medication is used as a single agent was removed. **Bone Cancer:** The requirements that the tumor is tumor mutational burden-high (TMB-H); the patient has progressed following prior treatment; and the medication is used in combination with Yervoy were removed. **Cervical Cancer:** The requirement that the patient has PD-L1 positive disease (CPS ≥ 1) was removed. The requirement of approval that the medication is used as second-line or subsequent therapy was modified to the medication is used as subsequent therapy. **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:** The requirement that the "patient has histologic transformation to diffuse large B-cell lymphoma" was modified to the "patient has histologic Richter transformation". The requirement that the patient meets ONE of the following: tumor has del(17p)/TP53 mutation; disease is chemotherapy refractory; or the patient is unable to receive chemoimmunotherapy were removed. The associated Note was also removed. The requirement that the medication is used as single agent or in combination with Imbruvica (ibrutinib capsules, tablets, or oral suspension) was removed.	

	Endometrial Carcinoma: The requirement that the medication will be used as a single agent was removed. The option for approval that the patient has TMB-H tumors was added. **Kaposi Sarcoma:** The requirement that the medication is used as a single agent or in combination with Yervoy was removed. **Merkel Cell Carcinoma:** The options for approval that the patient has primary or recurrent locally advanced disease and according to the prescriber, curative surgery and curative radiation therapy are not feasible were removed. The patient has in-transit regional disease was added as an option for approval. **Pediatric Diffuse High-Grade Gliomas:** Indication was changed to as listed. Previously, listed as diffuse high-grade gliomas. **Pediatric Hodgkin Lymphoma:** The following options for approval were removed: The medication is used for re-induction therapy in combination with Adcetris; the medication is used as a single-agent; the medication is used in combination with ICE. **Primary Mediastinal Large B-Cell Lymphoma:** The following options of approval were removed: The medication is used as a single agent; the medication is used in combination with Adcetris. **Small Bowel Adenocarcionoma:** The option of approval that the patient has advanced or metastatic disease and has NOT received prior checkpoint inhibitors was modified to the patient has advanced or metastatic disease. The corresponding Note was removed. **Small Cell Lung Cancer:** The requirement that the medication is used as second-line or subsequent therapy was modified to the medication is used as subsequent therapy. **Thyroid Carcinoma:** The requirement that the medication is used as a single agent was removed. **Vaginal Cancer:** The requirement that the patient has PD-L1 positive disease (CPS ≥ 1) was removed. The requirement that the medication is used as second-line or subsequent therapy was modified to the medication is used as subsequent therapy. **Vulvar Cancer:** The requirement that the patient has human papilloma virus (HPV)-related disease was removed. The requirement that the patient has advanced, recurrent, or metastatic disease was added.	
Selected Revision	**Classic Hodgkin Lymphoma:** The option that the medication is used as primary treatment was removed. The medication is used in combination with doxorubicin, vinblastine, and dacarbazine (AVD) or the patient is NOT a candidate for anthracycline therapy with the corresponding Note were added as options for approval **Pediatric Hogkin Lymphoma:** This condition was moved from "Other Uses with Supportive Evidence" to "FDA-Approved Indications." The option that the medication is used for primary therapy was modified to the patient has untreated disease. When the patient has relapsed and refractory disease, the option that the patient has tried at least one prior systemic chemotherapy and the corresponding Note was removed.	04/22/2026