UTILIZATION MANAGEMENT MEDICAL POLICY

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

REVIEW DATE: 08/06/2025

OVERVIEW

Opdivo, 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. 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 the confirmatory trials.
- **Colorectal cancer**:
  - For 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 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.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Opdivo. 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 as well as the monitoring required for adverse events and long-term efficacy, approval requires Opdivo 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 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, or iii):
- **i.** The medication is used as primary treatment and meets ONE of the following (a, b, or c):
  - **a)** The medication is used in combination with AVD; OR
    Note: AVD includes doxorubicin, vinblastine, dacarbazine.
  - **b)** The medication is used in combination with Adcetris (brentuximab intravenous infusion); OR
  - **c)** The medication is used as a single agent; OR
- **ii.** Patient has had an allogeneic hematopoietic stem cell transplantation (HSCT); OR
- **iii.** 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); 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 1 year 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, ii, or iii):
- **i.** Patient has tried chemotherapy; OR
  Note: Examples of chemotherapy are fluoropyrimidine such as 5-fluorouracil (5-FU), 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, medically inoperable, advanced, or metastatic disease; OR
- **iii.** 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.

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, iii, iv, or v):

i. Patient meets BOTH of the following (a and b):

a) Patient has received preoperative chemotherapy; AND
Note: Examples of chemotherapy include 5-fluorouracil plus either cisplatin or oxaliplatin; and paclitaxel plus carboplatin.

b) According to the prescriber, the patient has residual disease; OR

ii. Patient meets BOTH of the following (a and b):

a) Patient has squamous cell carcinoma; AND

b) Patient meets ONE of the following [(1), (2), or (3)]:

(1) According to the prescriber, the 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; OR

iii. Patient meets ALL of the following (a, b, c, d, and e):

a) Patient has adenocarcinoma; AND

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

(1) According to the prescriber, the patient is not a surgical candidate; OR

(2) Patient has unresectable locally advanced, recurrent, or metastatic disease; AND

c) The disease is negative for human epidermal growth factor receptor 2 (HER2) overexpression; AND

d) The tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 1; AND

e) The medication is used in combination with fluoropyrimidine and oxaliplatin; OR
Note: Examples of fluoropyrimidines include 5-fluorouracil and capecitabine.

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

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

(1) According to the prescriber, the patient is not a surgical candidate; OR

(2) Patient has unresectable locally advanced, recurrent, or metastatic disease; AND

b) The tumor is microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR); AND

c) The medication will be used in combination with ONE of the following [(1) or (2)]:

(1) Fluoropyrimidine and oxaliplatin containing chemotherapy; OR
Note: Examples of fluoropyrimidines include 5-fluorouracil and capecitabine.

(2) Yervoy (ipilimumab intravenous infusion); OR

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

a) Patient has adenocarcinoma; AND

b) The tumor is MSI-H or dMMR; AND

c) The medication is used as neoadjuvant or perioperative immunotherapy; 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.

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, ii, or iii):
- **i.** Patient meets ALL of the following (a, b, and c):
  - **a)** Patient has locoregional disease; 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
- **ii.** Patient meets ALL of the following (a, b, c, and d):
  - **a)** Patient meets ONE of the following [(1) or (2)]:
    - **(1)** Patient has unresectable locally advanced, unresectable locoregional, recurrent, or metastatic disease; OR
    - **(2)** According to the prescriber, the patient is not a surgical candidate; AND
  - **b)** The disease is negative for human epidermal growth factor receptor 2 (HER2) overexpression; AND
  - **c)** The tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 1; AND
  - **d)** The medication is used in combination with fluoropyrimidine and oxaliplatin; OR
    Note: Examples of fluoropyrimidines include fluorouracil and capecitabine.
- **iii.** Patient meets ALL of the following (a, b, and c):
  - **a)** Patient meets ONE of the following [(1) or (2)]:
    - **(1)** Patient has unresectable locally advanced, unresectable locoregional, recurrent, or metastatic disease; OR
    - **(2)** According to the prescriber, the patient is not a surgical candidate; AND
  - **b)** The tumor is MSI-H or dMMR; AND
  - **c)** Patient meets ONE of the following [(1) or (2)]:
    - **i.** The medication is used in combination with Yervoy (ipilimumab intravenous infusion); OR
    - **ii.** The medication is used in combination with a fluoropyrimidine and oxaliplatin; AND
      Note: Examples of fluoropyrimidines include fluorouracil and capecitabine.

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.

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.

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 Opdivo will be used as neoadjuvant treatment; OR
  - **iii.** Approve for up to 1 year (total) if Opdivo 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.

8. 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)** If used as first-line therapy, the medication is 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 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 II or 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; OR

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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, 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. 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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12. 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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13. 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
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 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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14. Anal 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 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. Patient meets BOTH of the following (a and b):
    a) The medication is used as subsequent therapy; AND
    b) Patient has NOT received prior checkpoint inhibitors; AND
    Note: Examples of checkpoint inhibitors include Keytruda (pembrolizumab intravenous infusion), Opdivo, Libtayo (cemiplimab intravenous infusion), Jemperli (dostarlimab intravenous infusion), Zynyx (retifanlimab-dlwr intravenous infusion), Loqtorzi (toripalimab-tpzi intravenous infusion), Tevimbra (tislelizumab-jsgr intravenous infusion).
D) The medication is 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) 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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15. 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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16. Bone Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, F, and G):
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 tumor is tumor mutational burden-high (TMB-H); AND
E) Patient has progressed following prior treatment; AND
F) The medication is used in combination with Yervoy (ipilimumab intravenous infusion); AND
G) 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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17. 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 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks.

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18. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. 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 histologic transformation to diffuse large B-cell lymphoma; AND
C) Patient meets ONE of the following (i, ii, or iii):
- **i.** Patient has del(17p)/TP53 mutation; OR
- **ii.** Patient is chemotherapy refractory; OR
  Note: An example of chemotherapy includes CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone).
- **iii.** Patient is unable to receive chemoimmunotherapy; AND
  Note: Examples of chemoimmunotherapy include RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) and OFAR (oxaliplatin, fludarabine, cytarabine, rituximab).

D) The medication is used as a single agent or in combination with Imbruvica (ibrutinib capsules, tablets, or oral suspension); AND
E) 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.

19. 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.

20. Endometrial 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 recurrent or metastatic disease; AND
- **C)** Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors; 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)** 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.

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23. Kaposi Sarcoma. 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 relapsed or refractory disease; AND
- **C)** The medication is used as a single agent or 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 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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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 locally advanced disease; AND
    - **b)** According to the prescriber, curative surgery and curative radiation therapy are not feasible; OR
  - **ii.** 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
  - **iii.** Patient has metastatic (disseminated) disease; AND
  - **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.

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 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 medication is used for primary treatment; AND
    - **d)** The medication is used in combination with doxorubicin, vinblastine, and dacarbazine (AVD); OR
  - **ii.** Patient meets ALL of the following (a, b, and c):
    - **a)** Patient has relapsed or refractory disease; AND
    - **b)** Patient has tried at least one prior systemic chemotherapy; AND
      Note: Examples of systemic chemotherapy are AVPC (doxorubicin, vincristine, prednisone, cyclophosphamide), ABVE-PC (doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide), OEPA (vincristine, etoposide, prednisone, doxorubicin).
    - **c)** Patient meets ONE of the following [(1), (2), or (3)]:
      - **(1)** The medication is used for re-induction therapy in combination with Adcetris (brentuximab intravenous infusion); OR
      - **(2)** The medication is used as a single-agent; OR
      - **(3)** The medication is used in combination with ifosfamide, carboplatin, and etoposide (ICE); 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.

28. Primary Mediastinal Large B-Cell Lymphoma. 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) Patient meets ONE of the following (i or ii):
i. The medication is used as a single agent; OR
ii. The medication is used in combination with Adcetris (brentuximab intravenous infusion); 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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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) 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
C) Patients meets ONE of the following (i or ii):
i. Patient has locally unresectable or medically inoperable disease; OR
ii. Patient has advanced or metastatic disease and has NOT received prior checkpoint inhibitors; AND
Note: Examples of checkpoint inhibitors include Keytruda (pembrolizumab intravenous infusion), Opdivo, Jemperli (dostarlimab-gxly intravenous infusion), Zynyx (retifanlimab-dlwr intravenous infusion), Loqtorzi (toripalimab-tpzi intravenous infusion), Libtayo (cemiplimab-rwlc intravenous infusion), Tevimbra (tislelizumab-jsgr).
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.

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)** 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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30. 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, 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 is 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 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, 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 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 human papilloma virus (HPV)-related 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 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.

REFERENCES

1. Opdivo® intravenous infusion [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; June 2025.
2. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 2.2025 – January 30, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 15, 2025.
3. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 15, 2025. Search term: nivolumab.
4. The NCCN Head and Neck Cancers Clinical Practice Guidelines in Oncology (version 4.2025 – June 20, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 15, 2025.
5. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (version 1.2025 – March 20, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 16, 2025.
6. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 2.2025 – January 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 16, 2025.
7. The NCCN Melanoma: Uveal Clinical Practice Guidelines in Oncology (version 1.2025 – February 11, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 16, 2025.
8. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 4.2025 – June 27, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 15, 2025.
9. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 2.2025 – March 31, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 15, 2025.

10. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 7.2025 – July 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 17, 2025.
11. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 3.2025 – January 9, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 16, 2025.
12. The NCCN Bladder Cancer Clinical Practice Guidelines in Oncology (version 1.2025 – March 25, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 16, 2025.
13. The NCCN Anal Carcinoma Clinical Practice Guidelines in Oncology (version 4.2025 – May 30, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
14. The NCCN Gestational Trophoblastic Neoplasia Cancer Clinical Practice Guidelines in Oncology (version 3.2025 – May 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
15. The NCCN Mesothelioma: Pleural Clinical Practice Guidelines in Oncology (version 2.2025 – January 14, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 16, 2025.
16. The NCCN Merkel Cell Carcinoma Clinical Practice Guidelines in Oncology (version 21.2025 – April 18, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
17. The NCCN Small Bowel Adenocarcinoma Clinical Practice Guidelines in Oncology (version 3.2025 – March 31, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
18. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – May 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
19. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 3.2025 – March 7, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
20. The NCCN Gastric Cancer Clinical Practice Guidelines in Oncology (version 2.2025 – April 4, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 15, 2025.
21. The NCCN Vulvar Cancer Clinical Practice Guidelines in Oncology (version 1.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
22. The NCCN Pediatric Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 2.2025 – June 9, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
23. The NCCN Esophageal and Esophagogastric Junction Cancers Clinical Practice Guidelines in Oncology (version 3.2025 – April 22, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 15, 2025.
24. The NCCN Cervical Cancer Clinical Practice Guidelines in Oncology (version 4.2025 – March 24, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
25. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2025 – June 3, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
26. The NCCN Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 4.2025 – January 13, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025, 2025.
27. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (version 2.2025 – May 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
28. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 2.2025 – February 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
29. The NCCN Pediatric Aggressive Mature B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – April 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
30. The NCCN Pediatric Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2025 – January 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
31. The NCCN Ampullary Adenocarcinoma Clinical Practice Guidelines in Oncology (version 2.2025 – January 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
32. The NCCN Kaposi Sarcoma Clinical Practice Guidelines in Oncology (version 2.2025 – January 14, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
33. The NCCN Mesothelioma: Peritoneal Clinical Practice Guidelines in Oncology (version 2.2025 – January 14, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 16, 2025.
34. The NCCN Biliary Tract Cancers Clinical Practice Guidelines in Oncology (version 2.2025 – July 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
35. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 1.2025 – May 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
36. The NCCN Vaginal Cancer Clinical Practice Guidelines in Oncology (version 5.2025 – February 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
37. The NCCN Pancreatic Adenocarcinoma Clinical Practice Guidelines in Oncology (version 2.2025 – February 3, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
38. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Cancer Clinical Practice Guidelines in Oncology (version 3.2025 – April 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.

39. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 1.2025 – March 27, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
40. The NCCN Squamous Cell Skin Cancer Clinical Practice Guidelines in Oncology (version 2.2025 – February 7, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.
41. Chan IS, Bhatia S, Kaufman HL, Lipson EJ. Immunotherapy for Merkel cell carcinoma: A turning point in patient care. *J Immunother Cancer*. 2018;6:23.
42. Schenker M, Burotto M, Richardet M, et al. CheckMate 848: A randomized, open-label, phase 2 study of nivolumab in combination with ipilimumab or nivolumab monotherapy in patients with advanced or metastatic solid tumors of high tumor mutational burden. *Cancer Res*. 2022;82(Suppl 12):CT022.
43. Klein O, Kee D, Markman B, et al. Immunotherapy of ipilimumab and nivolumab in patients with advanced neuroendocrine tumors: A subgroup analysis of the CA209-538 clinical trial for rare cancers. *Clin Cancer Res*. 2020;26:4454-4459.
44. Naumann RW, Hollebecque A, Meyer T, et al. Safety and efficacy of nivolumab monotherapy in recurrent or metastatic cervical, vaginal, or vulvar carcinoma: results from the phase I/II CheckMate 358 trial. *J Clin Oncol*. 2019;37:2825-2834.
45. Azad NS, Gray RJ, Overman MJ, et al. Nivolumab is effective in mismatch-deficient noncolorectal cancers: results from the Arm Z1D – A subprotocol of the NCI-MATCH (EAY131) study. *J Clin Oncol*. 2019;38:214-222.
46. Lheureux S, Matei DE, Konstantinopoulos PA, et al. Translational randomized phase II trial of cabozantinib in combination with nivolumab in advanced, recurrent, or metastatic endometrial cancer. *J Immunother Cancer*. 2022;Mar;10(3):e004233.
47. Younes A, Santoro A, Shipp M, et al. Nivolumab for classical Hodgkin lymphoma after autologous stem-cell transplantation and brentuximab vedotin failure: A prospective phase 2 multi-cohort study. *Lancet Oncol*. 2016;17:1283-1294.
48. Herrera AF, Moskowitz AJ, Bartlett NL, et al. Interim results of brentuxumab vedotin in combination with nivolumab in patients with relapsed or refractory Hodgkin lymphoma. *Blood*. 2018;131:1183-1194.
49. Zinzani PL, Santoro A, Gritti G, et al. Nivolumab combined with brentuximab vedotin for relapsed/refractory primary mediastinal large B-cell lymphoma: Efficacy and safety from the phase II CheckMate 436 study. *J Clin Oncol*. 2019;37:3081-3089.
50. Spigel DR, Vicente D, Ciuleanu TE, et al. Second-line nivolumab in relapsed small-cell lung cancer: CheckMate 331. *Ann Oncol*. 2021;32:631-641.
51. Ready NE, Ott PA, Hellman MD, et al. Nivolumab monotherapy and nivolumab plus ipilimumab in recurrent small cell lung cancer: Results from the CheckMate 032 randomized cohort. *J Thorac Oncol*. 2020;15:426-435.
52. Gordon EM, Chawla SP, Tellez WA, et al. SAINT: A Phase I/expended Phase II study using safe amounts of ipilimumab, nivolumab, and trabectedin as first-line treatment of advanced soft tissue sarcoma. *Cancers*. 2023;15:906.
53. Wagner MJ, Othus M, Patel SP, et al. Multicenter Phase II trial (SWOG S1609, cohort 51) of ipilimumab and nivolumab in metastatic or unresectable angiosarcoma: A substudy of dual anti-CTLA-4 and anti-PD-1 blockade in rare tumors (DART). *J Immunother Cancer*. 2021;9:e002990.
54. Schenker M, Burotto M, Richardet M, et al. ChackMate 848: A randomized, open-label, phase 2 study of nivolumab in combination with ipilimumab or nivolumab monotherapy in patients with advanced or metastatic solid tumors of high tumor mutational burden. *Cancer Reseacrh*. 2022;82:CT022-CT022.
55. Munhoz RR, Nader-Marta G, de Camargo VP, et al. A phase 2 study of first-line nivolumab in patients with locally advanced or metastatic cutaneous squamous-cell carcinoma. *Cancer*. 2022;128:4223-4231.
56. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 18, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Classic Hodgkin Lymphoma:** Added ICE (ifosfamide, carboplatin, and etoposide) to requirement that the patient has relapsed or refractory disease and the medication will be used in combination with Adcetris. **Colon, Rectal, or Appendiceal Cancer:** Added Appendiceal to the condition of approval. Added medication is used for adjuvant therapy as an approval option. **Esophageal and Esophagogastric Junction Carcinoma:** For squamous cell carcinoma, added according to the prescriber, the patient is not a surgical candidate, as an option of approval. Added locally and recurrent to patient has unresectable locally advanced, recurrent, or metastatic disease. Added requirement that the disease is negative for human epidermal growth factor 2 overexpression. **Head and Neck Squamous Cell Carcinoma:** Patient has progressed on or following platinum based chemotherapy was removed as an option for approval. **Mesothelioma:** For first-line therapy, added patient has unresectable disease as a requirement. **Non-Small Cell Lung Cancer:** Added first-line use in patients with recurrent, advanced, or metastatic disease with *BRAF V600E* mutation, *NTRK1/2/3* gene fusion, *MET* exon 14	02/08/2023

	skipping mutation, or *RET* rearrangement, in combination with Yervoy® (ipilimumab intravenous infusion) as an option of approval. Removed *BRAF V600E* mutation, *NTRK1/2/3* gene fusion, *MET* exon 14 skipping mutation, or *RET* rearrangement as options for approval for first-line or subsequent therapy. **Renal Cell Carcinoma:** Removed Stage IV from requirement that the patient has advanced, relapsed, or metastatic disease. For first-line therapy, added patient has clear cell histology as a requirement. **Ampullary Adenocarcinoma:** Added new condition of approval. **Anal Carcinoma:** Added 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks as another dosing option. **Bone Cancer:** Added new condition of approval. **Cervical Cancer:** Removed 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks as a dosing option. **Diffuse High-Grade Gliomas:** Added new condition of approval. **Endometrial Carcinoma:** Added 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks as a dosing option. **Extranodal NK/T-Cell Lymphomas:** Removed nasal type from the condition of approval. **Kaposi Sarcoma:** Added new condition of approval. **Merkel Cell Carcinoma:** Added 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks as another dosing option. **Primary Mediastinal Large B-Cell Lymphoma:** Added new condition of approval. **Vulvar Cancer:** Removed 480 mg as an intravenous infusion administered not more frequently than once every 3 weeks as a dosing option.	
Selected Revision	**Renal Cell Carcinoma:** Removed requirement "If used as first line therapy, the patient meets the following: the patient has clear cell histology; AND the medication is used in combination with Yervoy or Cabometyx.".	08/23/2023
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	01/31/2024

	(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.	
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), 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	02/12/2025

	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	08/06/2025

	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 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.	