Utilization Review Policy 177

POLICY: Oncology – Opdivo® (nivolumab injection for intravenous use – Bristol-Myers Squibb)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 01/31/2024

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW

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

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 three or more lines of systemic therapy that includes auto-HSCT.*
2) **Colorectal cancer**, with or without Yervoy® (ipilimumab intravenous infusion) for patients ≥ 12 years of age with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic disease that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.*
3) **Esophageal carcinoma**, in the following situations:
   - For patients with unresectable advanced, recurrent, or metastatic squamous cell disease after prior fluoropyrimidine- and platinum-based chemotherapy.
   - Adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in patients 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.
4) **Gastric cancer, esophagogastric junction cancer, and esophageal adenocarcinoma**, for patients with advanced or metastatic disease, in combination with fluoropyrimidine- and platinum-containing chemotherapy.
5) **Head and neck squamous cell carcinoma**, in patients with recurrent or metastatic disease with disease progression on or after platinum-based therapy.
6) **Hepatocellular carcinoma**, in patients who have been previously treated with Nexavar® (sorafenib tablets), in combination with Yervoy.*
7) **Malignant pleural mesothelioma**, for first-line treatment, in combination with Yervoy in adults with unresectable disease.
8) **Melanoma**, in patients with:
   - Unresectable or metastatic disease as a single agent.
   - Unresectable or metastatic disease in combination with Yervoy.
   - Adjuvant treatment for lymph node involvement or metastatic disease in patients who have undergone complete resection.
9) **Non-small cell lung cancer**:
   i. As first-line treatment in combination with Yervoy, in adults with metastatic disease expressing programmed death-ligand 1 (≥ 1%) as determined by an FDA-approved test, without epidermal growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations.

ii. As 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.
iii. In patients 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.
iv. In combination with platinum-doublet chemotherapy, as neoadjuvant treatment of adults with resectable (tumors ≥ 4 cm or node positive) disease.

10) **Renal cell carcinoma**:
i. In patients with advanced disease who have received prior anti-angiogenic therapy.
ii. In combination with Yervoy, for patients with intermediate or poor risk and previously untreated advanced disease.
iii. In combination with Cabometyx® (cabozantinib tablets), for the first-line treatment of patients with advanced disease.

11) **Urothelial carcinoma**, in the following situations:
- In patients with advanced or metastatic disease who have disease progression during or following platinum-containing chemotherapy.
- In patients with advanced or metastatic disease who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
- Adjuvant treatment of patients at high risk of recurrence after undergoing radical resection of urothelial carcinoma.

* This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

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

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 conditions (i, ii, iii, or iv):

i. Patient has had a hematopoietic stem cell transplantation (HSCT); OR
ii. Patient has tried three or more systemic regimens AND this includes an auto-HSCT as one line of therapy; OR
Note: Examples are ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine), Sanford V (doxorubicin, vinblastine, mechlorethamine, etoposide, vincristine, bleomycin, and prednisone), escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone).
iii. Patient has relapsed or refractory disease and the medication is used in combination with Adcetris (brentuximab intravenous infusion) or ICE (ifosfamide, carboplatin, and etoposide); OR
iv. Patient is not eligible for transplant according to the prescriber; 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.

---

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) The tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
C) Patient meets ONE of the following (i, ii, or iii):
A) 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).
B) Patient has unresectable, advanced, or metastatic disease; OR
C) 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, or C):
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.

---

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, or iv):
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 ALL of the following (a, b, and c):
a) Patient has squamous cell carcinoma; AND
b) Patient meets ONE of the following criteria [(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) Patient has tried chemotherapy; OR
Note: Examples of chemotherapy include fluoropyrimidines (5-fluorouracil [5-FU] and capecitabine) plus either cisplatin or oxaliplatin, paclitaxel plus carboplatin, or cisplatin plus either docetaxel or paclitaxel.

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 criteria [(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) has a combined positive score (CPS) ≥ 5; AND
- **e)** The medication is used in combination with fluoropyrimidine (fluorouracil or capecitabine) and oxaliplatin; OR

iv. Patient meets ALL of the following (a, b, c, d, and e):
- **a)** Patient has squamous cell carcinoma; AND
- **b)** Patient meets ONE of the following criteria [(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 medication will be used for first-line therapy; AND
- **e)** The medication will be used in combination with ONE of the following [(1) or (2)]:
  - **(1)** Fluoropyrimidine and platinum containing chemotherapy; OR
    Note: Examples of fluoropyrimidines include 5-fluorouracil and capecitabine and examples of platinum agents include cisplatin and carboplatin.
  - **(2)** Yervoy (ipilimumab intravenous infusion); AND

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

Dosing. Approve one of the following dosing regimens (A, B, 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, C, D, E, and F):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following (i or ii):
  - **i.** Patient has unresectable locally advanced, recurrent, or metastatic disease; OR
  - **ii.** According to the prescriber, the patient is not a surgical candidate; 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) has a combined positive score (CPS) ≥ 5; AND
- **E)** The medication is used in combination with fluoropyrimidine (fluorouracil or capecitabine) and oxaliplatin; 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) 360 mg as an intravenous infusion administered not more frequently than once every 3 weeks.

---

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 or ii):
~~a.~~ Patient has non-nasopharyngeal disease; OR
b. Patient meets ALL of the following conditions (a, b, and c):
i. Patient has nasopharyngeal disease; AND
ii. Patient has recurrent, unresectable, oligometastatic, or metastatic disease; AND
iii. Opdivo is used in combination with cisplatin and gemcitabine; 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, Including Hepatobiliary 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 tried at least one tyrosine kinase inhibitor; AND
Note: Examples are Nexavar (sorafenib tablets), Lenvima (lenvatinib capsules).
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 ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
i. Approve for 1 year if the patient has unresectable, advanced, or metastatic melanoma; OR
ii. Approve for up to 1 year of treatment (total) if Opdivo will be used as adjuvant treatment; AND
Note: Examples are in a patient with no evidence of disease following resection of node-positive disease, locoregional recurrence, or in-transit recurrence.
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.

---

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):
  A) Malignant pleural mesothelioma; OR
  B) Malignant peritoneal mesothelioma; OR
  C) Pericardial mesothelioma; OR
  D) Tunica vaginalis testis mesothelioma; AND
C) If used as first-line therapy, the patient meets the following (i and ii):
  A) The patient has unresectable disease; AND
  B) 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.

---

9. Non-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) Patient meets one of the following (i, ii, iii, iv, v, or vi):
  i. Opdivo is used as first-line or continuation maintenance therapy and the patient meets ALL of the following (a, b, and c):
    Note: This is regardless of programmed death-ligand-1 (PD-L1) status.
    a) Patient has recurrent, advanced, or metastatic disease; AND
    b) Opdivo will be used in combination with Yervoy (ipilimumab intravenous infusion); AND
    c) The tumor is negative for actionable mutations; OR
      Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (*EGFR*) mutation, anaplastic lymphoma kinase (*ALK*) fusions, *NTRK* gene fusion-positive, *ROS1, BRAF V600E, MET 14* skipping mutation, *RET* rearrangement.
  ii. Opdivo is used as first-line therapy and the patient meets ALL of the following (a, b, and c):
    Note: This is regardless of PD-L1 status.
    i. Patient has recurrent, advanced, or metastatic disease; AND
    ii. The tumor is positive for one of the following mutations [(1), (2), (3), or (4)]:
      1. *BRAF V600E* mutation; OR
      2. *NTRK1/2/3* gene fusion; OR
      3. *MET* exon 14 skipping mutation; OR
      4. *RET* rearrangement; AND
    iii. The medication will be used in combination with Yervoy (ipilimumab intravenous infusion); OR
  iii. Opdivo is used as first-line or subsequent therapy and the patient meets ALL of the following (a, b, and c):
    Note: This is regardless of PD-L1 status.
    i. Patient has recurrent, advanced, or metastatic disease; AND

ii. The tumor is positive for one of the following mutations [(1), (2), or (3)]:
1. Epidermal growth factor receptor (*EGFR*) exon 20 mutation; OR
2. *KRAS G12C* mutation; OR
3. *ERBB2* (*HER2*); AND

iii. The medication will be used in combination with Yervoy (ipilimumab intravenous infusion); OR

iv. Opdivo is used as subsequent therapy and the patient meets ALL of the following (a, b, c, and d):

a) Patient has recurrent, advanced, or metastatic disease; AND

b) The tumor is positive for one of the following mutations [(1), (2), (3), or (4)]:
1. Epidermal growth factor receptor (*EGFR*) *S768I, L861Q*, and/or *G719X* mutation positive; OR
2. *EGFR* exon 19 deletion or exon 21 L858R; OR
3. Anaplastic lymphoma kinase (*ALK*) rearrangement positive; OR
4. *ROS1* rearrangement positive; AND

c) The patient has received targeted drug therapy for the specific mutation; AND
Note: Examples of targeted drug therapy include Gilotrif (afatinib tablet), Tagrisso (osimertinib tablet), erlotinib, Iressa (gefitinib tablet), Vizimpro (dacomitinib tablet), Xalkori (crizotinib capsule), Rozlytrek (entrectinib capsule), or Zykadia (ceritinib tablet).

d) Opdivo is used in combination with Yervoy (ipilimumab intravenous infusion); OR

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

a) Patient has recurrent, advanced, or metastatic disease; AND

b) Patient has tried systemic chemotherapy; AND
Note: Examples of systemic chemotherapy include cisplatin, carboplatin, Alimta (pemetrexed injection), Abraxane (paclitaxel albumin-bound injection), gemcitabine, paclitaxel.

c) Patient has not progressed on prior therapy with a programmed death-1 (PD-1)/PD-L1 inhibitor; AND
Note: This includes previous therapy with either one of Opdivo, Keytruda (pembrolizumab intravenous infusion), or Tecentriq (atezolizumab intravenous infusion).

d) If tumor is positive for an actionable mutation, the patient has received targeted drug therapy for the specific mutation; AND
Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (*EGFR*) mutation, anaplastic lymphoma kinase (*ALK*) fusions, *NTRK* gene fusion-positive, *ROS1, BRAF V600E, MET 14* skipping mutation, *RET* rearrangement; OR

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

a) Patient has resectable disease; AND
Note: Resectable disease is defined as tumors ≥ 4 cm or node positive.

b) Opdivo is used as neoadjuvant therapy; AND

c) Opdivo is used in combination with platinum-doublet chemotherapy; AND
Note: Examples of platinum-doublet chemotherapy include carboplatin plus paclitaxel, cisplatin plus pemetrexed, and cisplatin plus gemcitabine.

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.

10. 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 advanced, relapsed, 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, 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.

---

11. Urothelial 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. Patient has tried at least one other chemotherapy regimen; OR
Note: Examples of chemotherapy regimens are cisplatin, carboplatin, gemcitabine.
ii. Patient is at high risk of recurrence after radical resection of the tumor; 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.

Other Uses with Supportive Evidence

---

12. 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) Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease; AND
C) Patient meets ONE of the following (i or ii):
i. The medication is used first-line and the patient has ONE of the following (a, b, or c):
a) Unresectable localized disease; OR
b) Stage IV resected disease; OR
c) Metastatic disease at initial presentation; 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.

---

13. Anal 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 tried at least one chemotherapy regimen; AND
Note: Examples of chemotherapy are 5-fluorouracil (5-FU), cisplatin, carboplatin plus paclitaxel, FOLFOX (oxaliplatin, leucovorin, and 5-FU).
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; OR
C) 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

---

14. Bone Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, F, G, and H):
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) Patient has tumor mutational burden-high (TMB-H) disease; AND
E) Patient has progressed following prior treatment; AND
F) Patient has no satisfactory alternative treatment options; AND
G) The medication is used in combination with Yervoy (ipilimumab intravenous infusion); AND
H) 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.

---

15. 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 programmed death ligand-1 (PD-L1) positive disease (combined positive score [CPS] ≥ 1); AND
C) The medication is used as second-line or 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.

---

16. 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.

---

17. Endometrial Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has tried at least one prior systemic therapy; AND
  Note: Examples are carboplatin, paclitaxel, docetaxel, cisplatin, doxorubicin, topotecan, ifosfamide, everolimus/letrozole.
- **C)** Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease; 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; OR
- **C)** 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

18. 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.

19. Gestational Trophoblastic Neoplasia. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient meets one of the following (i or ii):
  - **i.** Patient has tried at least one previous chemotherapy regimen for recurrent or progressive disease; OR
    Note: Examples of chemotherapy regimens contain etoposide, cisplatin/carboplatin, paclitaxel, bleomycin, ifosfamide, methotrexate.
  - **ii.** Patient has methotrexate-resistant high-risk 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)** 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

20. Kaposi Sarcoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient has classic disease; AND
- **B)** Patient has relapsed or refractory disease; AND
- **C)** 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 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks.

21. 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 or ii):
  - **i.** Patient has disseminated Merkel cell carcinoma; OR
  - **ii.** 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.

22. Neuroendocrine Tumors. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has advanced or metastatic disease; AND
- **C)** Patient meets one of the following (i or ii):
  - **i.** Patient has well differentiated, Grade 3 disease; OR
  - **ii.** Patient has poorly differentiated, large or small cell disease (other than lung); AND
- **D)** The medication 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.

23. Pediatric Hodgkin Lymphoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is < 18 years of age; AND
- **B)** Patient has tried at least one prior systemic chemotherapy; AND
  Note: Examples are AVPC (doxorubicin, vincristine, prednisone, cyclophosphamide), ABVE-PC (doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide), OEPA (vincristine, etoposide, prednisone, doxorubicin).
- **C)** If used for re-induction therapy, the medication is used in combination with Adcetris (brentuximab intravenous infusion); AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

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

---

24. 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) after a partial response to therapy for 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)** 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

---

25. 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 advanced or metastatic disease; AND
- **C)** The tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); 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.

---

26. 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 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. 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)** Patient has tried at least one prior systemic therapy; AND
  Note: Examples are cisplatin, carboplatin, fluorouracil, paclitaxel, bevacizumab.
- **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; February 2023.
2. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 2.2023 – November 8, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 31, 2023.
3. The NCCN Drugs & Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 30, 2023. Search term: nivolumab.
4. The NCCN Head and Neck Cancers Clinical Practice Guidelines in Oncology (version 1.2023 – December 20, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
5. The NCCN Hepatobiliary Cancer Clinical Practice Guidelines in Oncology (version 5.2022 – January 13, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
6. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 1.2023 – December 22, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 1, 2023.
7. The NCCN Uveal Melanoma Clinical Practice Guidelines in Oncology (version 2.2022 – April 5, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 30, 2023.
8. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 3.2022 – January 25, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
9. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 4.2022 – January 25, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
10. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 1.2023 – December 22, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 1, 2023.
11. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 1.2024 – June 21, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 18, 2023.
12. The NCCN Bladder Cancer Clinical Practice Guidelines in Oncology (version 3.2022 – December 21, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 1, 2023.
13. The NCCN Anal Carcinoma Clinical Practice Guidelines in Oncology (version 1.2023 – January 9, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 20231.
14. The NCCN Gestational Trophoblastic Neoplasia Cancer Clinical Practice Guidelines in Oncology (version 1.2023 – December 20, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
15. The NCCN Malignant Pleural Mesothelioma Clinical Practice Guidelines in Oncology (version 1.2023 – December 15, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
16. The NCCN Merkel Cell Carcinoma Clinical Practice Guidelines in Oncology (version 2.2022 – March 24, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 30, 2023.
17. The NCCN Small Bowel Adenocarcinoma Clinical Practice Guidelines in Oncology (version 1.2023 – January 9, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
18. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2023 – January 5, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 1, 2023.
19. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 1.2023 – December 22, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
20. The NCCN Gastric Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – January 11, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 31, 2023.
21. The NCCN Vulvar Cancer Clinical Practice Guidelines in Oncology (version 1.2023 – December 22, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 1, 2023.
22. The NCCN Pediatric Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 1.2023 – January 12, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
23. The NCCN Esophageal and Esophagogastric Junction Cancers Clinical Practice Guidelines in Oncology (version 5.2022 – December 5, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 31, 2023.
24. The NCCN Cervical Cancer Clinical Practice Guidelines in Oncology (version 1.2023 – January 6, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 1, 2023.
25. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2022 – September 29, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 31, 2023.

26. The NCCN Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2023 – December 21, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 1, 2023.
27. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (version 2.2022 – December 21, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 1, 2023.
28. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 2.2023 – September 28, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 31, 2023.
29. The NCCN Pediatric Aggressive Mature B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 3.2022 – October 19, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 31, 2023.
30. The NCCN Pediatric Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2023 – October 31, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 31, 2023.
31. The NCCN Ampullary Adenocarcinoma Clinical Practice Guidelines in Oncology (version 2.2022 – December 6, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 31, 2023.
32. The NCCN Kaposi Sarcoma Clinical Practice Guidelines in Oncology (version 1.2023 – December 20, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 31, 2023.
33. The NCCN Mesothelioma: Peritoneal Clinical Practice Guidelines in Oncology (version 1.2023 – December 15, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
34. 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.
35. 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.
36. 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.
37. 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.
38. 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.
39. 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.
40. 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Classic Hodgkin Lymphoma:** An option of approval was added that "the patient has relapsed or refractory disease and the medication is used in combination with Adcetris (brentuximab intravenous infusion)". **Colon or Rectal Cancer:** Removed Microsatellite Instability High (MSI-H) or Mismatch Repair Deficient (dMMR) from the condition of approval and added it as a requirement. Added "advanced" to option of approval that patient has unresectable or metastatic disease and removed "and is not a candidate for intensive therapy, according to the prescriber". **Esophageal and Esophagogastric Junction Carcinoma:** Removed "patient has residual disease following surgical resection" as an option of approval for both squamous cell carcinoma and adenocarcinoma. **Head and Neck Squamous Cell Carcinoma:** For non-nasopharyngeal disease, removed options of approval that "the patient has tried chemotherapy," or "platinum-containing chemotherapy or other chemotherapy is contraindicated". Added requirement that "the patient has progressed on platinum-based chemotherapy". Added options of approval that "the patient has nasopharyngeal disease", "has recurrent, unresectable, oligometastatic, or metastatic disease", and "Opdivo is used in combination with cisplatin and gemcitabine". **Mesothelioma:** Removed Malignant Pleural from the condition of approval. Removed requirement that "the patient has unresectable disease". Added "malignant pleural mesothelioma, malignant peritoneal mesothelioma, pericardial mesothelioma, and tunica vaginalis testis mesothelioma" as options of approval. Added "if used as first-line therapy" to requirement that Opdivo is used in combination with Yervoy. Added additional dosing regimen of up to 3 mg/kg as an intravenous infusion not more frequently than once every 2 weeks. **Melanoma:** Revised dosing regimen to from 1 mg/kg to 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks. **Non-Small Cell Lung Cancer:** Added "recurrent" to requirement that the patient has advanced or metastatic disease. Added "or continuation maintenance" to requirement that Opdivo is used first-line. Removed requirement that "the tumor expresses programmed death ligand-1 ≥ 1%" and added Note that this is regardless of PD-L1 status. Added "or subsequent" to requirement that Opdivo is used as first-line therapy. Revised requirement from the tumor is negative for actionable mutations to "the tumor is positive for one of the following mutations: epidermal growth factor receptor exon 20 mutation, KRAS G12C mutation, BRAF V600E mutation, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, or RET rearrangement". Removed requirement that Opdivo is used in combination with platinum-doublet chemotherapy. Added option of approval for subsequent therapy that "the tumor is epidermal growth factor receptor S768I, L861Q, and/or G719X mutation positive" or "ROS1 rearrangement positive", and "patient has received targeted therapy", and "Opdivo used in combination with Yervoy". **Cervical Cancer:** Added new condition of approval. **Endometrial Carcinoma:** Revised requirement from patient has progressed on, to "patient has tried at least one prior systemic therapy". Added "microsatellite instability-high" to requirement that patient has mismatch repair deficient disease. **Merkel Cell Carcinoma:** Added "the medication is used as neoadjuvant therapy" as an option of approval. **Neuroendocrine Tumors:** Added new conditional of approval. **Small Bowel Adenocarcinoma:** Removed "if the medication is used as initial therapy, the patient has tried oxaliplatin in the adjuvant setting or has a contraindication to oxaliplatin" and "the medication is used as subsequent therapy". **Small Cell Lung Cancer:** Added new condition of approval.	01/26/2022
Selected Revision	**Colon or Rectal Cancer:** Removed "up to" from 3 mg/kg dosing regimen. **Esophageal and Esophagogastric Junction Carcinoma:** Add criterion for the first-line treatment of adults with unresectable advanced or metastatic squamous cell carcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy or Yervoy (ipilimumab intravenous infusion). Added 360 mg as an intravenous (IV) infusion administered not more frequently than once every 3 weeks and 3 mg/kg as an IV infusion administered not more frequently than once every 2 weeks as additional dosing regimens.	07/13/2022

	Melanoma: Removed "up to" from 3 mg/kg dosing regimen. **Mesothelioma:** Removed "up to" from 3 mg/kg dosing regimen. **Non-Small Cell Lung Cancer:** Added criterion for neoadjuvant treatment of adults with resectable disease in combination with platinum-doublet chemotherapy. Removed "up to" from the 3 mg/kg dosing regimen. **Renal Cell Carcinoma:** Removed "up to" from 3 mg/kg dosing regimen.	
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 additional option for approval. **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 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.	02/08/2023
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 (ipilimumab intravenous infusion) or Cabometyx (cabozantinib tablets).".	08/23/2023