**OVERVIEW**

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

1) Melanoma, patients with:
   - unresectable or metastatic disease:
     - as a single agent
     - or in combination with Yervoy® (ipilimumab intravenous injection) in patients with melanoma; * AND
   - the adjuvant setting, in patients with lymph node involvement or metastatic disease who have undergone complete resection; AND

2) Non-small cell lung cancer (NSCLC), patients with:
   - metastatic disease and progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo; AND

3) Small cell lung cancer, in patients with metastatic disease with progression after platinum-based chemotherapy and at least one other line of therapy; ** AND

4) Renal cell carcinoma (RCC):
   - Patients with advanced disease who have received prior anti-angiogenic therapy; AND
   - In combination with Yervoy, for patients with intermediate or poor risk and previously untreated advanced RCC; AND

5) Classical Hodgkin lymphoma (cHL), for adults that have relapsed or progressed after** autologous hematopoietic stem cell transplantation (auto-HSCT) and Adcetris® (brentuximab vedotin intravenous injection) OR three or more lines of systemic therapy that includes auto-HSCT; AND

6) Squamous cell head and neck (SCCHN) carcinoma, in patients with recurrent or metastatic disease with disease progression on or after platinum-based therapy; AND

7) Urothelial carcinoma, in patients with advanced or metastatic disease who:**
   - have disease progression during or following platinum-containing chemotherapy; OR
   - who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; AND

8) Colorectal cancer (mCRC), ± Yervoy 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; ** AND

9) Patients with hepatocellular carcinoma (HCC) who have been previously treated with Nexavar® (sorafenib tablets), **

* This indication is approved under accelerated approval based on progression-free survival (PFS). Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.
**This indication is approved under accelerated approval based on overall response rate (ORR) 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 conditions of coverage in the **Criteria** and **Dosing** for the listed indication(s). Extended approvals are allowed if the patient continues to meet the criteria and dosing. All approvals are provided for the duration noted below.

*Indications with a ^ below are also covered (and, if applicable, further detailed/referenced) in the corresponding Commercial Care Continuum (CC) Policy. Note: Additional criteria requirements for coverage of the same indication as outlined in the Commercial CC Policy and this Medicare Advantage CC Policy may NOT be the same.*

*Indications noted with eviCore are managed by eviCore healthcare for those clients who use eviCore for oncology and/or oncology-related reviews. For these indications, a prior authorization should be initiated through eviCore at www.eviCore.com.*

**RECOMMENDED AUTHORIZATION CRITERIA**

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

**FDA-Approved Indications**

1. **Classical Hodgkin Lymphoma (cHL). ^ eviCore**

**Criteria.** Approve for 1 year if the patient meets ONE of the following criteria (A, B, or C):
   A) The patient has had a hematopoietic stem cell transplantation (HSCT); OR
   B) The patient has tried three or more systemic regimens AND this includes an auto-HSCT as one line of therapy
      Note: Examples are ABVD [doxorubicin, bleomycin, vinblastine, and dacarbazine], Sanford V [doxorubicin, vinblastine, mechloethamine, etoposide, vincristine, bleomycin, and prednisone], escalated BEACOPP [bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone]; OR
   C) The patient is not eligible for transplant according to the prescriber.

**Dosing.** Approve the following dosing regimens:
   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. **Head and Neck Squamous Cell Carcinoma (HNSCC). ^ eviCore**

**Criteria.** Approve for 1 year if the patient meets BOTH of the following criteria (A and B):
   A) The patient has non-nasopharyngeal HNSCC; AND
   B) The patient meets ONE of the following conditions (i or ii):
      i. The patient has tried chemotherapy.
      Note: Examples of chemotherapy are cisplatin, carboplatin, Erbitux® [cetuximab intravenous infusion], 5-fluorouracil [5-FU], capecitabine, paclitaxel, docetaxel, methotrexate [MTX]); OR
ii. A platinum-containing chemotherapy regimen or other chemotherapy is contraindicated, according to the prescriber.

Dosing. Approve the following dosing regimens:
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.

3. Hepatocellular Carcinoma (HCC), Including Hepatobiliary Cancers.  

Criteria. Approve for 1 year if the patient has tried at least one tyrosine kinase inhibitor (TKI) [e.g., Nexavar (sorafenib tablets), Lenvima (levatinib capsules)].

Dosing. Approve the following dosing regimens:
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.

4. Melanoma.  

Criteria. The patient must meet ONE of the following (A or B):
A) Approve for 1 year if the patient has unresectable, advanced, or metastatic melanoma; OR
B) Approve for up to 1 year of treatment (total) if Opdivo will be used as adjuvant treatment (e.g., in a patient with no evidence of disease following resection of node-positive disease, locoregional recurrence, or in transit recurrence).

Dosing. Approve the following dosing regimens:
A) 240 mg administered not more frequently than once every 2 weeks as an intravenous infusion; OR
B) 480 mg administered not more frequently than once every 4 weeks as an intravenous infusion; OR
C) Up to 1 mg per kg administered not more frequently than once every 3 weeks as an intravenous infusion.

5. Colon or Rectal Cancer, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR).  

Criteria. Approve for 1 year if the patient meets BOTH of the following criteria (A and B):
A) The patient is 12 years of age or greater; AND
B) One of the following applies (i or ii):
   i. The patient has tried chemotherapy.
      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]); OR
   ii. The patient has unresectable or metastatic disease and is not a candidate for intensive therapy, according to the prescriber.

Dosing. Approve the following dosing regimens:
A) 240 mg administered as an intravenous infusion not more frequently than once every 2 weeks; OR
B) Up to 3 mg/kg administered as an intravenous infusion not more frequently than once every 2 or 3 weeks.
6. Non-Small Cell Lung Cancer (NSCLC). \(^{eviCore}\)

**Criteria.** Approve for 1 year if the patient meets ALL of the following criteria (A, B, and C):

A) The patient has tried systemic chemotherapy (e.g., cisplatin, carboplatin, Alimta [pemetrexed injection], Abraxane [paclitaxel albumin-bound injection], gemcitabine, paclitaxel); AND

B) The patient has not progressed on prior therapy with a programmed death-1 (PD-1)/PD-ligand 1 (PD-L1) inhibitor.

Note: This includes previous therapy with either one of Opdivo, Keytruda (pembrolizumab for injection), or Tecentriq (atezolizumab for injection); AND

C) If non-squamous cell carcinoma (that is, adenocarcinoma, large cell, or NSCLC not otherwise specified) AND the patient’s tumor is positive for a targetable mutation (i.e., sensitizing epidermal growth factor receptor [**EGFR**] mutation, anaplastic lymphoma kinase [**ALK**] fusions), the patient has received targeted drug therapy for the specific mutation.

**Dosing.** Approve the following dosing regimens:

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.

7. Renal Cell Carcinoma (RCC). \(^{eviCore}\)

**Criteria.** Approve for 1 year if the patient has advanced (e.g., relapsed, Stage IV, or metastatic) disease.

**Dosing.** Approve one of the following dosing regimens:

A) 240 mg administered not more frequently than once every 2 weeks as an intravenous infusion; OR

B) 480 mg administered not more frequently than once every 4 weeks as an intravenous infusion; OR

C) Up to 3 mg per kg administered not more frequently than once every 3 weeks as an intravenous infusion.

8. Small Cell Lung Cancer (SCLC). \(^{eviCore}\)

**Criteria.** Approve for 1 year if the patient has tried at least one other chemotherapy regimen.

Note: Examples of chemotherapy are cisplatin, carboplatin, etoposide irinotecan, topotecan, paclitaxel.

**Dosing.** Approve one of the following dosing regimens:

A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR

B) Up to 3 mg/kg intravenously administered not more frequently than once every 2 weeks; OR

C) Up to 3 mg/kg intravenously administered not more frequently than once every 4 weeks.

9. Urothelial Cancer. \(^{eviCore}\)

**Criteria.** Approve for 1 year if the patient has tried at least one other chemotherapy regimen.

Note: Examples of chemotherapy regimens are cisplatin, carboplatin, gemcitabine, Keytruda [pembrolizumab IV infusion], Tecentriq [atezolizumab IV infusion]).

**Dosing.** Approve the following dosing regimens:

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

10. Anal Carcinoma. ^ eviCore

Criteria. Approve for 1 year if the patient has received other chemotherapy.
Note: Examples of chemotherapy are 5-fluorouracil [5-FU], cisplatin, carboplatin plus paclitaxel, FOLFOX [oxaliplatin, leucovorin, and 5-FU]).

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

11. Gestational Trophoblastic Neoplasia. ^ eviCore

Criteria. Approve for 1 year if the patient meets one of the following (A or B):
A) The patient has tried at least one previous chemotherapy regimen for recurrent or progressive disease.
   Note: Examples of chemotherapy regimens contain etoposide, cisplatin/carboplatin, paclitaxel, bleomycin, ifosfamide, methotrexate; OR
B) The patient has methotrexate-resistant high-risk disease.

Dosing. Approve one of the following dosing regimens:
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.

12. Malignant Pleural Mesothelioma. ^ eviCore

Criteria. Approve for 1 year if the patient has tried first-line chemotherapy
Note: Examples of chemotherapy are Alimta [pemetrexed] plus cisplatin or carboplatin, Alimta with cisplatin and bevacizumab, gemcitabine plus cisplatin, Alimta alone, vinorelbine).

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

13. Merkel Cell Carcinoma. ^ eviCore

Criteria. Approve for 1 year if the patient has disseminated Merkel cell carcinoma

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

14. Small Bowel Adenocarcinoma. ^ eviCore

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Criteria. Approve for 1 year if the patient meets the following criteria (A and B):
A) The patient has advanced or metastatic disease that is deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H); AND
B) The patient meets one of the following criteria (i or ii):
   i. If the medication is used as initial therapy, the patient has tried oxaliplatin in the adjuvant setting or has a contraindication to oxaliplatin; OR
   ii. The medication will be used as subsequent therapy.

Dosing. Approve one of the following doses:
A) 3 mg per 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; OR
C) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Opdivo has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Disease Progression While Receiving Another PD-1 Directed Agent (e.g., pembrolizumab). Note: If the PD-1 directed agent was discontinued for reasons other than disease progression, then Opdivo may be approved if other requirements for coverage are met.

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

REFERENCES
SEE COMMERCIAL CARE CONTINUUM POLICY FOR FULL LIST OF REFERENCES