MEDICAL MUTUAL®

Drug Policy

Policy:	**201511-CC**	**Initial Effective Date: 03/16/2015** **Annual Review Date: 02/21/2019** **Last Revised Date: 02/21/2019**
Code(s):	**HCPCS J9299**	
SUBJECT:	**Opdivo® (nivolumab injection for intravenous use)**	

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

OVERVIEW

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

1) Melanoma, patients with:
   - unresectable or metastatic disease:
     - as a single agent in patients with *BRAF V600* wild-type melanoma; AND
     - as a single agent in patients with *BRAF V600* mutation positive melanoma;* AND
     - 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, in the adjuvant setting; 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
This policy involves the use of Opdivo. Prior authorization is recommended for medical benefit coverage of Opdivo. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. The requirement that the patient meet the Criteria for coverage of the requested medication applies to the initial authorization only. **Waste Management** applies for all covered conditions. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Opdivo as well as the monitoring required for adverse events (AEs) and long-term efficacy, initial approval requires Opdivo be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

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

FDA-Approved Indications

1. **Classic Hodgkin Lymphoma (cHL).** Approve for 6 months if the patient meets BOTH of the following (A and B):
   - **A)** ONE the following conditions applies (i, ii, or iii):[2]
     - **i.** The patient has had a hematopoietic stem cell transplantation (HSCT); OR
     - **ii.** The patients has tried three or more systemic regimens (e.g., 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]) AND this includes an auto-HSCT as one line of therapy; OR
     - **iii.** The patient is not eligible for transplant according to the prescribing physician.
   - **B)** Opdivo is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens:
A) 240 mg as an intravenous infusion given once every 2 weeks;[1] OR
B) 480 mg as an intravenous infusion given once every 4 weeks.

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2. Head and Neck Squamous Cell Carcinoma (HNSCC). Approve for 6 months if the patient meets ALL of the following (A, B, and C):
~~**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 (e.g., 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 prescribing physician; AND
C) Opdivo is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens:
A) 240 mg as an intravenous infusion given once every 2 weeks; OR
B) 480 mg as an intravenous infusion given once every 4 weeks.

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3. Hepatocellular Carcinoma (HCC), Including Hepatobiliary Cancers. Approve for 6 months if the patient meets BOTH of the following (A and B):
A) The patient has tried at least one tyrosine kinase inhibitor (TKI) [e.g., Nexavar {sorafenib tablets}, Lenvima {levatinib capsules}];[1,6] AND
B) Opdivo is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens:
A) 240 mg as an intravenous infusion given once every 2 weeks; OR
B) 480 mg as an intravenous infusion given once every 4 weeks.

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4. Melanoma [NOTE: This includes cutaneous melanoma, brain metastases due to melanoma, and uveal melanoma]. Approve for the duration noted if the patient meets BOTH of the following (A and B):
A) The patient meets ONE of the following (i or ii):
a. Approve for 6 months if the patient has unresectable, advanced, or metastatic melanoma; OR

b. Approve for 6 months (up to 1 year of total treatment) 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); AND

B) Opdivo is prescribed by or in consultation with an oncologist; AND

Dosing. Approve the following dosing regimens

A) 240 mg every 2 weeks as an intravenous infusion; OR

B) 480 mg every 4 weeks as an intravenous infusion; OR

C) Up to 1 mg per kg once every 3 weeks as an intravenous infusion.

The recommended dose is 240 mg IV Q2W or 480 mg Q4W until disease progression or unacceptable toxicity.[1] When given in combination with Yervoy, the dose is 1 mg/kg given Q3W for 4 doses, followed by Opdivo 240 mg as a single agent Q2W OR Opdivo 480 mg Q4W. For adjuvant treatment of melanoma, Opdivo is given until disease recurrence or unacceptable toxicity for up to 1 year.

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5. Colon or Rectal Cancer, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR). Approve for 6 months if the patient meets ALL of the following (A, B, and C):

A) The patient is 12 years of age or greater;[1] AND

B) One of the following applies (i or ii):[18-19]

i. The patient has tried chemotherapy (e.g., a 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 prescribing physician.

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

Dosing. Approve the following dosing regimens:

A) 240 mg as an intravenous infusion once every 2 weeks; OR

B) Up to 3 mg/kg as an intravenous infusion given once every 2 or 3 weeks.

The recommended dose in adults and children ≥ 12 years of age is 240 mg given as an intravenous infusion over 30 minutes every 2 weeks until disease progression or unacceptable toxicity.[1] When given in combination with Yervoy, the dose is 3 mg/kg given Q3W for 4 doses, followed by Opdivo 240 mg as a single agent Q2W. Management of AEs may require that Opdivo be withheld or permanently discontinued as determined by the prescribing physician.

6. **Non-Small Cell Lung Cancer (NSCLC)**. Approve for 6 months if the patient meets ALL of the following (A, B, and C):
   - **A)** Opdivo is prescribed by or in consultation with an oncologist; AND
   - **B)** The patient has tried systemic chemotherapy (e.g., cisplatin, carboplatin, Alimta [pemetrexed injection], Abraxane [paclitaxel albumin-bound injection], gemcitabine, paclitaxel); AND
   - ~~**C)**~~ If non-squamous cell carcinoma (that is, adenocarcinoma, large cell, or NSCLC not otherwise specified) the patient must meet ONE of the following conditions (i or ii):
     - ~~**i.**~~ The patient's tumor is positive for a targetable mutation (i.e., sensitizing epidermal growth factor receptor [*EGFR*] mutation, anaplastic lymphoma kinase [*ALK*] fusions) AND the patient has received targeted drug therapy for the specific mutation; OR
     - ~~**ii.**~~ The tumor is negative or unknown for these targetable mutations (i.e., *EGFR, ALK)*.

   Dosing. Approve the following dosing regimens:
   - **A)** 240 mg as an intravenous infusion given once every 2 weeks; OR
   - **B)** 480 mg as an intravenous infusion given once every 4 weeks.

7. **Renal Cell Carcinoma (RCC).** Approve for 6 months if the patient meets BOTH of the following (A and B):
   - **A)** The patient has advanced (e.g., relapsed, Stage IV, or metastatic) renal cell carcinoma (RCC); AND
   - **B)** Opdivo is prescribed by or in consultation with an oncologist.

   Dosing. Approve the following dosing regimens:
   - **A)** 240 mg every 2 weeks as an intravenous infusion; OR
   - **B)** 480 mg every 4 weeks as an intravenous infusion; OR
   - **C)** Up to 3 mg per kg given every 3 weeks as an intravenous infusion.

   The recommended dose is 240 mg IV Q2W or 480 mg Q4W until disease progression or unacceptable toxicity.[1] When given in combination with Yervoy, the dose is 3 mg/kg given Q3W for 4 doses, followed by Opdivo 240 mg as a single agent Q2W OR Opdivo 480 mg Q4W.

8. **Small Cell Lung Cancer (SCLC).** Approve for 6 months if the patient meets BOTH of the following (A and B):
   - **A)** The patient has tried at least one systemic chemotherapy (e.g., cisplatin, carboplatin, etoposide) within the past 6 months; AND
   - **B)** Opdivo is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens:
A) 240 mg as an intravenous infusion given once every 2 weeks; OR
B) Up to 3 mg/kg intravenously given once every 2 weeks; OR
C) Up to 3 mg/kg intravenously given once every 4 weeks.

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9. Urothelial Carcinoma. Approve for 6 months if the patient meets BOTH of the following (A and B):
A) The patient has tried at least one other systemic therapy (e.g., cisplatin, carboplatin, gemcitabine, Keytruda [pembrolizumab IV infusion], Tecentriq [atezolizumab IV infusion]); AND
B) Opdivo is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens:
A) 240 mg as an intravenous infusion given once every 2 weeks; OR
B) 480 mg as an intravenous infusion given once every 4 weeks.

Other Uses With Supportive Evidence

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10. Anal Carcinoma. Approve for 6 months if the patient meets BOTH of the following (A and B):
A) The patient has received other chemotherapy (e.g., 5-fluorouracil [5-FU], cisplatin, carboplatin plus paclitaxel, FOLFOX [oxaliplatin, leucovorin, and 5-FU]); AND
B) Opdivo is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens:
A) 240 mg as an intravenous infusion given once every 2 weeks; OR
B) 3 mg per kg as an intravenous infusion given once every 2 weeks.

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11. Malignant Pleural Mesothelioma. Approve for 6 months if the patient meets BOTH of the following (A and B):
A) The patient has tried first-line chemotherapy (e.g., Alimta [pemetrexed] plus cisplatin or carboplatin, Alimta [pemetrexed] with cisplatin and Avastin [bevacizumab], gemcitabine plus cisplatin, Alimta alone, vinorelbine); AND
B) Opdivo is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 3 mg per kg as an intravenous infusion ~~over 60 minutes~~ once every 2 weeks.[35]

12. **Merkel Cell Carcinoma**. Approve for 6 months if the patient meets BOTH of the following (A and B):
    A) The patient has disseminated Merkel cell carcinoma; AND
    B) Opdivo is prescribed by or in consultation with an oncologist.

    Dosing. Approve 3 mg per kg as an intravenous infusion once every 2 weeks.[38-39]

13. **Other Cancer-Related Indications.** Forward to the Medical Director for review on a case-by-case basis. Other indications supported in the *NCCN Compendium* include T-cell lymphoproliferative disorders, extranodal NK/T-cell lymphoma, nasal type (category 3), chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) [2A], gestational trophoblastic neoplasia (2A).

Waste Management for All Indications.
The dose should be calculated and the number of vials needed assessed. Dosing for Opdivo as a single agent in patients with melanoma, NSCLC, RCC, cHL, SCCHN, urothelial carcinoma, and HCC is 240 mg or 480 mg. In CRC, Opdivo dosing as a single agent is 240 mg. When used in combination with Yervoy for melanoma or RCC, the dose of Opdivo is based on body weight (mg/kg). For Other Uses with Supportive Evidence, the dose is usually in mg/kg of body weight. The number of vials needed should be calculated and the entire vials are used. For other uses, see the dosing sections.

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. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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MEDICAL MUTUAL®

Drug Policy

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Code J9299.

HCPCS Code(s):	
J9299	Injection, nivolumab, 1 mg