SPECIALTY GUIDELINE MANAGEMENT

OPDIVO (nivolumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Unresectable or Metastatic Melanoma
   Opdivo (nivolumab), as a single agent or in combination with ipilimumab, is indicated for the treatment of patients with unresectable or metastatic melanoma.

2. Adjuvant Treatment of Melanoma
   Opdivo is indicated for the adjuvant treatment of patients with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.

3. Metastatic Non-Small Cell Lung Cancer
   Opdivo is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with 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.

4. Small Cell Lung Cancer
   Opdivo is indicated for the treatment of patients with metastatic small cell lung cancer (SCLC) with progression after platinum-based chemotherapy and at least one other line of therapy.

5. Advanced Renal Cell Carcinoma
   a. Opdivo as a single agent is indicated for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.
   b. Opdivo, in combination with ipilimumab, is indicated for the treatment of patients with intermediate or poor risk, previously untreated advanced RCC.

6. Classical Hodgkin Lymphoma
   Opdivo is indicated for the treatment of adult patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after:
   a. Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
   b. 3 or more lines of systemic therapy that includes autologous HSCT.

7. Squamous Cell Carcinoma of the Head and Neck
   Opdivo (nivolumab) is indicated for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

8. Urothelial Carcinoma
Opdivo is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:
a. Have disease progression during or following platinum-containing chemotherapy
b. Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

9. Microsatellite Instability-High or Mismatch Repair Deficient Metastatic Colorectal Cancer
Opdivo, as a single agent or in combination with ipilimumab, is indicated for the treatment of adult and pediatric patients 12 years and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

10. Hepatocellular Carcinoma
Opdivo, as a single agent or in combination with ipilimumab, is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

B. Compendial Uses
1. Cutaneous melanoma
2. Non-small cell lung cancer
3. Kidney cancer
4. Classical Hodgkin lymphoma
5. Squamous cell carcinoma of the head and neck
6. Urothelial carcinoma
   a. Bladder cancer
   b. Primary carcinoma of the urethra
   c. Upper genitourinary tract tumors
   d. Urothelial carcinoma of the prostate
7. Colorectal cancer
8. Small cell lung cancer
9. Hepatocellular carcinoma
10. Uveal Melanoma
11. Anal Carcinoma
12. Merkel Cell Carcinoma
13. Central Nervous System (CNS) brain metastases
14. Gestational trophoblastic neoplasia
15. Malignant pleural mesothelioma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION
Submission of the following information is necessary to initiate the prior authorization review: documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.

III. EXCLUSIONS
Coverage will not be provided for members who have experienced disease progression while on programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor therapy (other than when used as second-line or subsequent therapy for metastatic or unresectable melanoma in combination with ipilimumab following progression on single agent checkpoint inhibitor therapy).

IV. CRITERIA FOR INITIAL APPROVAL
A. Cutaneous Melanoma
Authorization of 6 months may be granted for treatment of cutaneous melanoma in either of the following settings:
1. Opdivo will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) for unresectable or metastatic disease.
2. Opdivo will be used as a single agent as adjuvant treatment following complete lymph node resection or complete resection of metastatic disease.

B. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted for treatment of NSCLC when either of the following conditions is met:
1. Opdivo will be used as a single agent as subsequent therapy for recurrent, advanced, or metastatic disease.
2. Opdivo will be used as a single agent or in combination with ipilimumab for treatment of disease with tumor mutational burden (TMB).

C. Kidney Cancer
Authorization of 6 months may be granted for treatment of relapsed, advanced, or stage IV kidney cancer, including renal cell carcinoma, in any of the following settings:
1. Opdivo will be used as a single agent for clear cell histology as subsequent therapy.
2. Opdivo will be used as a single agent for non-clear cell histology.
3. Opdivo will be used in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) for:
   i. First-line therapy for poor or intermediate risk.
   ii. First-line therapy for clear cell histology and favorable risk.
   iii. Subsequent therapy for clear cell histology.

D. Classical Hodgkin Lymphoma (cHL)
Authorization of 6 months may be granted for treatment of classical Hodgkin lymphoma when either of the following criteria is met:
1. Opdivo will be used as a single agent and the member meets one of the following criteria:
   i. Member has relapsed after 2 or more prior lines of therapy or following hematopoietic stem cell transplant.
   ii. Member has relapsed or refractory disease and is transplant-ineligible.
2. Opdivo will be used in combination with brentuximab vedotin for relapsed or refractory disease.

E. Squamous Cell Carcinoma of the Head and Neck (SCCHN)
Authorization of 6 months may be granted as a single agent for subsequent treatment of recurrent, unresectable, metastatic, or second primary SCCHN in members with disease progression on or after platinum-containing chemotherapy.

F. Urothelial Carcinoma – Bladder Cancer
Authorization of 6 months may be granted as a single agent as subsequent therapy for treatment of bladder cancer following platinum-containing chemotherapy when either of the following conditions is met:
1. Disease is locally advanced or metastatic.
2. Member has metastatic or local recurrence post-cystectomy.

G. Urothelial Carcinoma – Primary Carcinoma of the Urethra
Authorization of 6 months may be granted as a single agent as subsequent therapy for treatment of primary carcinoma of the urethra for recurrent, locally advanced, or metastatic disease following platinum-containing chemotherapy.
H. Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate
Authorization of 6 months may be granted as a single agent as subsequent therapy for treatment of upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate following platinum-containing chemotherapy for locally advanced or metastatic disease.

I. Colorectal Cancer
Authorization of 6 months may be granted for treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma for microsatellite-instability high or mismatch repair deficient tumors when any of the following criteria are met:
1. Opdivo will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) as primary treatment for unresectable metastatic disease following previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months.
2. Opdivo will be used as a single agent as initial therapy for unresectable advanced or metastatic disease in members who are not appropriate for intensive therapy.
3. Opdivo will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) as subsequent therapy for unresectable advanced or metastatic disease following previous oxaliplatin-irinotecan- and/or fluoropyrimidine-based therapy.

J. Small Cell Lung Cancer
Authorization of 6 months may be granted for subsequent treatment of small cell lung cancer in any of the following settings:
1. Opdivo will be used as a single agent or in combination with ipilimumab for relapse within 6 months following complete or partial response or stable disease with initial treatment.
2. Opdivo will be used as a single agent or in combination with ipilimumab for primary progressive disease.
3. Opdivo will be used for metastatic disease following progression after platinum-based chemotherapy and at least one other line of therapy.

K. Hepatocellular Carcinoma
Authorization of 6 months may be granted as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) for subsequent treatment of hepatocellular carcinoma.

L. Uveal Melanoma
Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for treatment of uveal melanoma for distant metastatic disease.

M. Anal Carcinoma
Authorization of 6 months may be granted as a single agent for second-line or subsequent treatment of metastatic anal carcinoma.

N. Merkel Cell Carcinoma
Authorization of 6 months may be granted for treatment of Merkel cell carcinoma in members with disseminated, metastatic disease.

O. CNS Brain Metastases
Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for treatment of CNS brain metastases in patients with melanoma.

P. Gestational Trophoblastic Neoplasia
Authorization of 6 months may be granted as a single agent for treatment of gestational trophoblastic neoplasia when either of the following criteria is met:

1. Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum/etoposide-containing regimen.
2. Member has methotrexate-resistant high-risk disease.

Q. Malignant Pleural Mesothelioma
Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for subsequent treatment of malignant pleural mesothelioma.

V. CONTINUATION OF THERAPY

A. Adjuvant treatment of melanoma
Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for cutaneous melanoma who have not experienced disease recurrence or an unacceptable toxicity.

B. All other indications
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who have not experienced disease progression or an unacceptable toxicity.

VI. REFERENCES