Opdivo (nivolumab)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Opdivo (nivolumab) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. Opdivo (nivolumab) is a human immunoglobulin G4 (IgG4) monoclonal antibody that bind to the P-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor response.

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.

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, in combination with ipilimum, is indicated for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1 (≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

Opdivo, in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy, is indicated for the first-line treatment of adult patients with metastatic or recurrent NSCLC, with no EGFR or ALK genomic tumor aberrations.

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. Malignant Pleural Mesothelioma
   Opdivo, in combination with ipilimumab, is indicated for the treatment of adult patients with unresectable malignant pleural mesothelioma, as first-line treatment.

6. 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.

7. 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.

8. 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.

9. 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.

10. 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.

11. 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.

12. Esophageal Squamous Cell Carcinoma
    Opdivo is indicated for the treatment of patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

<u>Compendial Uses</u>

1. Cutaneous melanoma
2. Non-small cell lung cancer
3. Renal cell carcinoma
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
16. Small bowel adenocarcinoma
17. Extranodal NK/T-cell lymphoma, nasal type

POLICY

Required 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.

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).

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).
3. Opdivo will be used in combination with ipilimumab for treatment of recurrent, advanced, or metastatic disease when used following EGFR or ALK therapy if EGFR or ALK positive.
4. Opdivo will be used in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy for treatment of recurrent, advanced, or metastatic disease when used following EGFR or ALK therapy if EGFR or ALK positive.

C. Renal Cell Carcinoma

Authorization of 6 months may be granted for treatment of relapsed, advanced, or stage IV 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 very advanced 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.
3. Member has muscle invasive local recurrence or persistent disease in a preserved bladder.

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 appendiceal carcinoma, 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 metachronous metastases and 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 for unresectable 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 advanced or metastatic disease following previous oxaliplatin- irinotecan- and/or fluoropyrimidine-based therapy.

J. Small Bowel Adenocarcinoma

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for treatment of advanced or metastatic small bowel adenocarcinoma for microsatellite-instability high or mismatch repair deficient tumors when either of the following criteria are met:

1. Opdivo will be used as subsequent therapy.
2. Opdivo will be used as initial therapy following prior adjuvant oxaliplatin exposure or contraindication to oxaliplatin.

K. 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.

L. 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.

M. 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.

N. Anal Carcinoma

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

O. Merkel Cell Carcinoma

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

P. CNS Brain Metastases

Authorization of 6 months may be granted for treatment of CNS brain metastases when either of the following criteria are met

1. Opdivo will be used as a single agent or in combination with ipilimumab in members with melanoma.
2. Opdivo will be used as a single agent in members with PD-L1 positive non-small cell lung cancer.

Q. Gestational Trophoblastic Neoplasia

Authorization of 6 months may be granted as a single agent for treatment of gestational trophoblastic neoplasia for multiagent chemotherapy-resistant disease 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 high-risk disease.

R. Malignant Pleural Mesothelioma
Authorization of 6 months may be granted for the treatment of malignant pleural mesothelioma in either of the following settings:
1. Opdivo will be used as first line therapy in combination with ipilimumab.
2. Opdivo will be used as subsequent therapy as a single agent or in combination with ipilimumab.

S. Esophageal Squamous Cell Carcinoma
Authorization of 6 months may be granted for subsequent therapy as a single agent for treatment of unresectable, recurrent or metastatic esophageal squamous cell carcinoma.

T. Extranodal NK/T-Cell Lymphoma, Nasal Type
Authorization of 6 months may be granted for treatment of relapsed or refractory extranodal NK/T-cell lymphoma, nasal type.

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. Non-small cell lung cancer
Authorization of 6 months may be granted (up to 24 months total when used in combination with ipilimumab) for continued treatment in members requesting reauthorization for non-small cell lung cancer who have not experienced disease progression or an unacceptable toxicity.

C. 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.

Opdivo is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J9299- Injection, nivolumab
- C9453- Injection, nivolumab

REFERENCES

- Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; June 2020.
- The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 21, 2020.

POLICY HISTORY

Policy #: 05.20.52
Original Effective Date: December 6, 2018
Reviewed: October 2020
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