Reference number(s)
2345-A

STANDARD MEDICARE PART B 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, in combination with ipilimumab, 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. 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.

5. Advanced Renal Cell Carcinoma
   i. 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.
   ii. Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of patients with intermediate or poor risk advanced RCC.
   iii. Opdivo, in combination with cabozantinib, is indicated for the first-line treatment of patients with 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:
i. Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
ii. Three 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:
i. Have disease progression during or following platinum-containing chemotherapy
ii. 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 is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously been treated with sorafenib.

11. Esophageal Cancer
Opdivo is indicated for the adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in patients who have received neoadjuvant chemoradiotherapy (CRT).

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.

12. Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma
Opdivo, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the treatment of patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma.

B. Compendial Uses
1. Cutaneous melanoma
2. Non-small cell lung cancer
3. Colorectal cancer
4. Urothelial carcinoma
   i. Bladder cancer
   ii. Primary carcinoma of the urethra
   iii. Upper genitourinary tract tumors
   iv. Urothelial carcinoma of the prostate
5. Renal cell carcinoma
6. Head and neck cancer
   i. Very advanced head and neck cancer

ii. Mucosal melanoma
7. Classical Hodgkin lymphoma
8. Hepatocellular carcinoma
9. Uveal melanoma
10. Anal carcinoma
11. Merkel cell carcinoma
12. Central nervous system (CNS) brain metastases
13. Malignant pleural mesothelioma
14. Gestational trophoblastic neoplasia
15. Diffuse large B-cell lymphoma
    i. Primary mediastinal large B-cell lymphoma
    ii. Histologic (Richter's) transformation to diffuse large B-cell lymphoma
16. Small bowel adenocarcinoma, including advanced ampullary cancer
17. Extranodal NK/T-cell lymphoma, nasal type
18. Poorly differentiated neuroendocrine carcinoma/Large or small cell carcinoma
19. Endometrial carcinoma
20. Vulvar squamous cell carcinoma
21. Gastric cancer
22. Esophageal and esophagogastric junction cancers
23. Hepatobiliary cancers – Biliary tract cancers
    i. Gallbladder cancer
    ii. Intrahepatic cholangiocarcinoma
    iii. Extrahepatic cholangiocarcinoma

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
1. Documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.
2. Documentation of molecular testing for EGFR and ALK genomic tumor aberrations, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 12 months may be granted for treatment of cutaneous melanoma in either of the following settings:
1. For treatment of unresectable or metastatic disease.
2. Opdivo will be used as adjuvant treatment of stage III or IV disease following complete resection or no evidence of disease.

B. Non-Small Cell Lung Cancer

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC when any of the following conditions is met:
1. Opdivo will be used as a single agent as subsequent therapy.
2. Opdivo will be used in combination with ipilimumab, if no EGFR or ALK genomic tumor aberrations (unless testing is not feasible due to insufficient tissue).

3. Opdivo will be used in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy, if no EGFR or ALK genomic tumor aberrations (unless testing is not feasible due to insufficient tissue).

C. Colorectal Cancer
Authorization of 12 months may be granted for treatment of colorectal cancer when both of the following criteria are met:
1. Disease is unresectable, advanced, metastatic, or inoperable.
2. Tumor is microsatellite instability-high or mismatch repair deficient.

D. Urothelial Carcinoma
Authorization of 12 months may be granted for treatment of urothelial carcinoma, including bladder cancer, upper genitourinary tract tumors, urothelial carcinoma of the prostate, and primary carcinoma of the urethra.

E. Renal Cell Carcinoma
Authorization of 12 months may be granted for treatment of renal cell carcinoma for relapsed, advanced or stage IV disease.

F. Head and Neck Cancer
Authorization of 12 months may be granted for treatment of head and neck cancer, including very advanced head and neck cancer and mucosal melanoma.

G. Classical Hodgkin Lymphoma
Authorization of 12 months may be granted for the treatment of classical Hodgkin lymphoma.

H. Hepatocellular Carcinoma
Authorization of 12 months may be granted for treatment of hepatocellular carcinoma.

I. Uveal Melanoma
Authorization of 12 months may be granted for treatment of uveal melanoma.

J. Anal Carcinoma
Authorization of 12 months may be granted for treatment of anal carcinoma.

K. Merkel Cell Carcinoma
Authorization of 12 months may be granted for treatment of Merkel cell carcinoma.

L. CNS Brain Metastases
Authorization of 12 months may be granted for treatment of CNS brain metastases in patients with melanoma or NSCLC.

M. Malignant Pleural Mesothelioma
Authorization of 12 months may be granted for 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.

N. Gestational Trophoblastic Neoplasia
Authorization of 12 months may be granted for treatment of gestational trophoblastic neoplasia.

O. Diffuse Large B-Cell Lymphoma
Authorization of 12 months may be granted for treatment of either of the following:

1. Primary mediastinal large B-cell lymphoma
2. Histologic (Richter's) transformation to diffuse large B-cell lymphoma.

P. Esophageal and Esophagogastric Junction Carcinoma

Authorization of 12 months may be granted for treatment of esophageal and esophagogastric junction carcinoma when any of the following criteria are met:

1. As subsequent therapy as a single agent for treatment of unresectable locally advanced, recurrent or metastatic squamous cell carcinoma.
2. As postoperative therapy following preoperative chemoradiation and complete tumor resection, when there is residual pathologic disease.
3. For treatment of adenocarcinoma in members who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease when the requested medication will be used in combination with chemotherapy.

Q. Small Bowel Adenocarcinoma

Authorization of 12 months may be granted for treatment of small bowel adenocarcinoma, including advanced ampullary cancer, when both of the following criteria are met:

1. Disease is advanced or metastatic.
2. Tumor is microsatellite-instability high or mismatch repair deficient.

R. Extranodal NK/T-Cell Lymphoma, Nasal Type

Authorization of 12 months may be granted for treatment of extranodal NK/T-cell lymphoma, nasal type.

S. Poorly Differentiated Neuroendocrine Carcinoma/Large or Small Cell Carcinoma

Authorization of 12 months may be granted for treatment of non-pancreatic neuroendocrine tumors.

T. Endometrial Carcinoma

Authorization of 12 months may be granted for treatment of endometrial carcinoma.

U. Vulvar Squamous Cell Carcinoma

Authorization of 12 months may be granted for treatment of HPV-related vulvar squamous cell carcinoma.

V. Gastric Cancer

Authorization of 12 months may be granted for treatment of gastric cancer in members who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease when the requested medication will be used in combination with chemotherapy.

W. Hepatobiliary Cancers – Biliary Tract Cancers

Authorization of 12 months may be granted for treatment of biliary tract cancers, including gallbladder cancer, intrahepatic cholangiocarcinoma, and extrahepatic cholangiocarcinoma.

IV. CONTINUATION OF THERAPY

A. Adjuvant Treatment of Melanoma

Authorization for 12 months total therapy may be granted for all members (including new members) who are continuing with Opdivo therapy when all of the following criteria are met:

1. The member is currently receiving therapy with Opdivo.
2. Opdivo is being used as adjuvant treatment for a member with melanoma.
3. The member is receiving benefit from therapy. Benefit is defined as:
   i. No evidence of unacceptable toxicity while on the current regimen AND
   ii. No evidence of disease recurrence while on the current regimen.

B. Non-Small Cell Lung Cancer or Malignant Pleural Mesothelioma

Authorization for 12 months may be granted (up to 24 months total when used in combination with ipilimumab) for all members (including new members) who are continuing with Opdivo therapy when all of the following criteria are met:

1. The member is currently receiving therapy with Opdivo.
2. The member is receiving benefit from therapy. Benefit is defined as:
    i. No evidence of unacceptable toxicity while on the current regimen AND
    ii. No evidence of disease progression while on the current regimen.

C. Renal Cell Carcinoma

Authorization for 12 months may be granted (up to 24 months total when used in combination with cabozantinib) for all members (including new members) who are continuing with Opdivo therapy when all of the following criteria are met:

1. The member is currently receiving therapy with Opdivo.
2. The member is receiving benefit from therapy. Benefit is defined as:
    i. No evidence of unacceptable toxicity while on the current regimen AND
    ii. No evidence of disease progression while on the current regimen.

D. Gastric Cancer, Esophageal Cancer, and Esophagogastric Junction Carcinoma

Authorization of 12 months may be granted (up to 24 months total when used in combination with chemotherapy; up to 12 months total when used as postoperative therapy for completely resected esophageal cancer or esophagogastric junction carcinoma) for all members (including new members) who are continuing with Opdivo therapy when all of the following criteria are met:

1. The member is currently receiving therapy with Opdivo.
2. The member is receiving benefit from therapy. Benefit is defined as:
    i. No evidence of unacceptable toxicity while on the current regimen AND
    ii. No evidence of disease progression while on the current regimen.

E. All Other Indications

Authorization for 12 months may be granted for all members (including new members) who are continuing with Opdivo therapy when all of the following criteria are met:

1. The member is currently receiving therapy with Opdivo.
2. Opdivo is being used to treat any other diagnosis or condition enumerated in Section III.
3. The member is receiving benefit from therapy. Benefit is defined as:
    i. No evidence of unacceptable toxicity while on the current regimen AND
    ii. No evidence of disease progression while on the current regimen.

V. REFERENCES

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2021.
2. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 21, 2021.