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 treatment of patients with intermediate or poor risk, previously untreated advanced RCC.
   iii. Opdivo, in combination with cabozantinib, is indicated for the first-line treatment of 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 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.

B. Compendial Uses
1. Cutaneous melanoma
2. Non-small cell lung cancer
3. Colorectal cancer
4. Urothelial carcinoma
5. Renal cell carcinoma
6. Head and neck cancer
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
16. Small bowel adenocarcinoma
17. Extranodal NK/T-cell lymphoma, nasal type
18. Poorly Differentiated Neuroendocrine Carcinoma/Large or Small Cell Carcinoma
19. Primary mediastinal large B-cell lymphoma
20. Endometrial Carcinoma
21. Vulvar Squamous Cell Carcinoma
22. Gastric Cancer
23. Esophageal/Esophagogastric Junction Cancers

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 programmed death ligand 1 (PD-L1) tumor expression, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 12 months may be granted for the 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 the treatment of NSCLC when either of the following conditions is met:

1. For treatment of recurrent, advanced, or metastatic disease.
2. Opdivo will be used for treatment of disease with tumor mutational burden (TMB).

C. Colorectal Cancer

Authorization of 12 months may be granted for the 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 the 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 the 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 the treatment of head and neck cancer.

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 the 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.

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 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, 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 first-line treatment of HER-2 negative adenocarcinoma in members who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease, when the tumor is PD-L1 positive [Combined Positive Score (CPS ≥5)] and 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 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. Primary Mediastinal Large B-cell Lymphoma
Authorization of 12 months may be granted for treatment of primary mediastinal large B-cell lymphoma.

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

V. Vulvar Squamous Cell Carcinoma
Authorization of 12 months may be granted for treatment of HPV-related vulvar squamous cell carcinoma.

W. Gastric Cancer

Authorization of 12 months may be granted for first-line treatment of HER-2 negative gastric adenocarcinoma in members who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease when the tumor is PD-L1 positive [Combined Positive Score (CPS ≥5)] and the requested medication will be used in combination with chemotherapy.

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 or
   ii. No evidence of disease recurrence while on the current regimen.

B. 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 or
   ii. No evidence of disease progression while on the current regimen.

C. 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:
   ii. No evidence of unacceptable toxicity while on the current regimen or
   iii. No evidence of disease progression while on the current regimen.

V. REFERENCES

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; January 2021.
2. The NCCN Drugs & Biologics Compendium® © 2020 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed January 22, 2021.