Clinical Policy: Nivolumab (Opdivo)

Reference Number: PA.CP.PHAR.121
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for nivolumab (Opdivo®).

FDA Approved Indication(s)
Opdivo is indicated for the treatment of:

- Patients with BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent.
- Patients with BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent.
- Patients with unresectable or metastatic melanoma, in combination with ipilimumab.
- Patients with melanoma with lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting.
- Patients with metastatic non-small cell lung cancer and 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.
- Patients with advanced renal cell carcinoma who have received prior antiangiogenic therapy.
- Adult patients with classical Hodgkin lymphoma that has relapsed or progressed after:
  - autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
  - 3 or more lines of systemic therapy that includes autologous HSCT.
- Patients with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy.
- Patients with locally advanced or metastatic urothelial carcinoma who:
  - have disease progression during or following platinum-containing chemotherapy;
  - have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
- Adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
- Patients with hepatocellular carcinoma who have been previously treated with sorafenib.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Opdivo is **medically necessary** when one of the following criteria are met:

I. Initial Approval Criteria

A. Melanoma (must meet all):

1. Diagnosis of unresectable or metastatic melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Dose does not exceed (a or b):

a. As a single agent: 240 mg every 2 weeks;
b. In combination with ipilimumab: 1 mg/kg for 4 doses, followed by 240 mg every 2 weeks.

Approval duration: 6 months

B. Non-Small Cell Lung Cancer (must meet all):
1. Diagnosis of metastatic non-small cell lung cancer (NSCLC);
2. Prescribed by or in consultation with an oncologist;
3. Member has experienced disease progression on or after platinum-based chemotherapy;
   a. If known epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) mutations, disease progression on one of the following (1 or 2):
      i. FDA-approved therapy if EGFR mutation status is positive (e.g., erlotinib, afatinib, gefitinib, osimertinib);
      ii. FDA-approved therapy if ALK mutation status is positive (e.g., crizotinib, ceritinib, alectinib, brigatinib);
4. Dose does not exceed 240 mg every 2 weeks.

Approval duration: 6 months

C. Renal Cell Carcinoma (must meet all):
1. Diagnosis of renal cell carcinoma (RCC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Meets a or b:
   a. FDA-approved use: advanced RCC and has received prior anti-angiogenic therapy;
   b. Off-label NCCN recommended use:
5. Systemic therapy as a single agent for non-clear cell histology;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 240 mg every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 6 months

D. Classical Hodgkin Lymphoma (must meet all):
1. Diagnosis of classical Hodgkin lymphoma;
2. Prescribed by or in consultation with an oncologist;
3. Meets a or b:
   a. FDA-approved use meets one of the following (i or ii):
      i. Disease has relapsed or progressed after autologous hematopoietic stem cell transplantation and post-transplantation brentuximab vedotin;
      ii. Disease has relapsed or progressed after 3 or more lines of systemic therapy that includes autologous hematopoietic stem cell transplantation;

b. Off-label NCCN recommended use, as a single agent for one of the following:
   i. Palliative treatment for age > 60 years if previously treated with brentuximab vedotin;
   ii. Treatment of relapsed disease or refractory disease for age ≥ 18 years if one of the following (1 or 2);
      1. Deauville 4-5;
      2. Previously treated with brentuximab vedotin;

4. Request meets one of the following (a or b):
   a. Dose does not exceed 240mg every 2 weeks or 480mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 6 months

E. Squamous Cell Carcinoma of the Head and Neck (must meet all):
1. Diagnosis of squamous cell carcinoma of the head or neck;
2. Prescribed by or in consultation with an oncologist;
3. Disease is recurrent or metastatic;
4. Disease has progressed on or after platinum-based chemotherapy;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 240mg every 2 weeks or 480mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 6 months

F. Urothelial Carcinoma (must meet all):
1. Diagnosis of urothelial carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Meets a or b:
   a. FDA-approved use:
      i. Disease is locally advanced or metastatic and (a or b):
         a) Disease has progressed during or following platinum-based chemotherapy;
         b) Disease has progressed within 12 months of neoadjuvant or adjuvant treatment with platinum-based chemotherapy;
   b. Off-label NCCN recommended use:
      1) As a single agent for the treatment of bladder cancer recurrence post cystectomy;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 240 mg every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 6 months

G. Colorectal Cancer (must meet all):

1. Diagnosis of MSI-H or defective mismatch repair (dMMR) colorectal cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Disease is unresectable or metastatic;
5. Member has had disease progression following treatment with a fluoropyrimidine (e.g., fluorouracil, capecitabine), oxaliplatin, and irinotecan;
6. Dose does not exceed 240 mg every 2 weeks.

Approval duration: 6 months

H. Hepatocellular Carcinoma (must meet all):

1. Diagnosis of hepatocellular carcinoma;
2. Member has compensated cirrhosis demonstrated by Child Pugh class A or B;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Member has had disease progression following treatment with sorafenib;
6. Dose does not exceed 240 mg every 2 weeks.

Approval duration: 6 months

I. Malignant Pleural Mesothelioma (off-label) (must meet all)**:**

1. Diagnosis of malignant pleural mesothelioma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member has failed initial treatment (i.e., platinum [cisplatin, carboplatin]-based chemotherapy, pemetrexed or vinorelbine);
5. Request is for use as a single agent or in combination with ipilimumab;
6. Dose is supported by practice guidelines or peer-reviewed literature for malignant pleural mesothelioma *(prescriber must submit supporting evidence).*

Approval duration: 6 months

J. Small Cell Lung Cancer (off-label) (must meet all):

1. Diagnosis of small cell lung cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member meets a or b:
   a. Member is experiencing a relapse within 6 months following complete or partial response or stable disease with initial treatment (i.e., platinum [cisplatin, carboplatin]-based chemotherapy);
   b. Member has primary progressive disease;
5. Request is for use as a single agent or in combination with ipilimumab;
6. Dose is supported by practice guidelines or peer-reviewed literature for small cell lung cancer *(prescriber must submit supporting evidence).*

Approval duration: 6 months

K. Other diagnoses/indications: Refer to PA. CP.PHAR.53

II. Continued Approval

A. All Indications (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (e.g., no disease progression or significant toxicity);
3. If request is for a dose increase, request meets one of the following (a or b):
    a. New dose does not exceed 3 mg/kg every 2 weeks;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PHAR.53

**American Joint committee on Cancer (AJCC) TNM staging classification (7th ed., 2010) as reported in NCCN Head and Neck Cancers: Stage IVB is equivalent to T4b (very advanced primary tumor), any N (regional lymph node status), M0 (no metastasis); as reported in NCCN Bladder Cancer: T4b or T2-4a, N1-3 disease are subcategories of Stage IV disease; T (primary tumor characteristics), N (regional lymph node status), M (metastasis status).*

Background

Description/Mechanism of Action:

Nivolumab is a human immunoglobulin G4 (IgG4) monoclonal antibody that binds to the programmed death receptor-1 (PD-1) and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. Binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells inhibits T-cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumors and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumors. In syngeneic mouse tumor models, blocking PD-1 activity resulted in decreased tumor growth.

Formulations:

Single dose vial for Injection:

- 40 mg/4 mL (10 mg/mL); 100 mg/10 mL (10 mg/mL) solution

Appendices

Appendix A: Abbreviation Key

ALK: anaplastic lymphoma kinase
BRAF: B-Raf proto-oncogene, serine/threonine kinase
EGFR: epidermal growth factor receptor
PD-1: programmed death receptor-1
ULN: upper limit of normal

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9299	Injection, nivolumab, 1 mg

Reviews, Revisions, and Approvals	Date	Approval Date
Added requirement for being prescribed by or in consultation with an oncologist; added requirement for Child-Pugh classification to for HCC indication; updated melanoma criteria set to reflect expanded indication for the adjuvant treatment of patients with melanoma: removed "unresectable or metastatic" from the diagnosis. Added coverage criteria for the new FDA-approved indication of hepatocellular carcinoma. Updated off-label usage requirements for NSCLC, RCC, Classical Hodgkin lymphoma, squamous cell carcinoma of the head and neck and urothelial carcinoma to reflect off-label NCCN recommendations for use. Added coverage criteria for the new FDA-approved indication of MSI-H/dMMR colorectal cancer and for the NCCN-recommended off-label usages of malignant pleural mesothelioma and small cell lung cancer. References reviewed and updated.	02/18	

References

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v. Kidney cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed August 28, 2017.
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x. Small cell lung cancer (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed August 28, 2017.
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