

## Clinical Policy: Nivolumab (Opdivo)

Reference Number: CP.PHAR.121

Effective Date: 07/15

Last Review Date: 04/17

[Coding Implications](#)  
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

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

### Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation® 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. Meets a or b:
  - a. FDA approved use (i or ii):
    - i. Single agent for BRAF V600 wild-type (no mutation) or BRAF V600 mutation-positive disease;
    - ii. In combination with ipilimumab;
  - b. NCCN recommended use:
    - i. Single agent or in combination with ipilimumab as (a, b or c):
      - a) First-line therapy;
      - b) Second-line or subsequent therapy for disease progression;
      - c) Re-induction therapy.

**Approval duration: 3 months**

##### B. Non-Small Cell Lung Cancer (must meet all):

1. Diagnosis of metastatic non-small cell lung cancer (NSCLC);
2. Meets a or b:
  - a. FDA approved use: disease progression on or after platinum-based chemotherapy (if known EGFR or ALK mutations, disease progression on an FDA-approved therapy for these mutations);
  - b. NCCN recommended use (i and ii):
    - i. NSCLC histology characterized as adenocarcinoma (with mixed subtypes), squamous cell carcinoma or large cell carcinoma;
    - ii. As single agent subsequent therapy for metastatic disease (a or b):
      - a) Following progression on a first-line cytotoxic regimen;
      - b) For further progression on other systemic therapy.

**Approval duration: 3 months**

**C. Renal Cell Carcinoma** (must meet all):

1. Diagnosis of renal cell carcinoma (RCC);
2. Meets a or b:
  - a. FDA approved use: advanced RCC and has received prior anti-angiogenic therapy;
  - b. NCCN recommended use (i or ii):
    - i. Subsequent therapy as a single agent for relapsed disease or for surgically unresectable stage IV disease with predominant clear cell histology;
    - ii. Systemic therapy as a single agent for non-clear cell histology.

**Approval duration: 3 months**

**D. Classical Hodgkin Lymphoma** (must meet all):

1. Diagnosis of classical Hodgkin lymphoma;
2. Meets a or b:
  - a. FDA approved use: disease has relapsed or progressed after autologous hematopoietic stem cell transplantation and post-transplantation brentuximab vedotin;
  - b. NCCN recommended use, as a single agent for one of the following:
    - i. Palliative treatment in members > 60 years of age;
    - ii. Treatment of relapsed disease or refractory disease in members  $\geq$  18 years of age.

**Approval duration: 3 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. Meets a or b:
  - a. FDA approved use: disease is recurrent or metastatic and has progressed on or after platinum-based chemotherapy;
  - b. NCCN recommended use:
    - i. Single agent for non-nasopharyngeal cancer with disease progression on or after platinum-based chemotherapy and any of the following:
      - a) Newly diagnosed stage IVB\* disease;
      - b) Unresectable nodal disease with no metastasis;
      - c) Disease not amenable to surgery;
      - d) Second primary tumor with prior radiation therapy.

**Approval duration: 3 months**

**F. Urothelial Carcinoma** (must meet all):

1. Diagnosis of urothelial carcinoma;
2. 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. NCCN recommended use:
  - i. As a single agent for any of the following:
    - a) Bladder cancer:
      - 1) For clinical stage T4b or T2-4a, N1-3 disease\*;
      - 2) For recurrence post cystectomy;
      - 3) For metastatic disease as subsequent systemic therapy;
    - b) Primary carcinoma of the urethra as subsequent systemic therapy for recurrent or metastatic disease
    - c) Upper genitourinary track tumor as subsequent systemic therapy for metastatic disease
    - d) Urothelial carcinoma of the prostate as subsequent systemic therapy for metastatic disease.

**Approval duration: 3 months**

**G. Other diagnoses/indications:** Refer to CP.PHAR.57 - Global Biopharm Policy.

- 1. The following NCCN recommended uses, meeting NCCN categories 1, 2a, or 2b, are approved per the CP.PHAR.57 Global Biopharm Policy:
  - a. Colon cancer;
  - b. Rectal cancer;
  - c. Small cell lung cancer.

**II. Continued Approval**

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

- 1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
- 2. No disease progression or unacceptable toxicity.

**Approval duration: 6 months**

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

- 1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
- 2. Refer to CP.PHAR.57 - Global Biopharm Policy.

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*\*American Joint committee on Cancer (AJCC) TNM staging classification (7<sup>th</sup> 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 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.

***FDA Approved Indications:***

Opdivo is a PD-1 blocking antibody/intravenous injectable formulation indicated for:

- Melanoma
  - BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent
  - BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent
  - Unresectable or metastatic melanoma, in combination with ipilimumab
- Lung cancer
  - 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
- Renal cell carcinoma
  - Advanced renal cell carcinoma who have received prior anti-angiogenic therapy
- Classical Hodgkin lymphoma
  - Classical Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation HSCT and posttransplantation brentuximab vedotin
- Squamous cell carcinoma of the head and neck
  - Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy
- Urothelial carcinoma
  - 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

**Appendices****Appendix A: Abbreviation Key**

ALK: anaplastic lymphoma kinase	NCCN: National Comprehensive Cancer Network
BRAF: B-Raf proto-oncogene, serine/threonine kinase	PD-1: programmed death receptor-1
EGFR: epidermal growth factor receptor	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
Policy developed.	07/15	07/15
Policy converted to new template. Melanoma: removed BRAF mutation requirement and previous trial/failure requirement of ipilimumab/BRAF inhibitor therapy per FDA labeling. NSCLC: removed squamous histologic type requirement and added requirement for previous trial/failure of targeted therapy for patients with EGFR or ALK mutations per FDA labeling; broadened previous trial/failure requirement from platinum-based chemo to first-line cytotoxic therapy per NCCN guidelines. Created criteria for advanced RCC and Hodgkin lymphoma per FDA labeling and per NCCN guidelines/compendia. Updated reasons to discontinue per FDA labeling.	05/16	06/16
Two new labeled indications added: head and neck cancer and urothelial carcinoma (NCCN compendial uses added for both indications and for colorectal and small cell lung cancer). RCC NCCN recommended uses edited to include non-clear histology; for clear cell, “after tyrosine kinase inhibitor therapy” deleted. Safety criteria removed if not a contraindication or black box warning not covered by a REMS program. Reference to performance status removed.	03/17	04/17

**References**

1. Opdivo prescribing information. Princeton, NJ: Bristol-Myers Squibb; February 2017. Available at [http://packageinserts.bms.com/pi/pi\\_opdivo.pdf](http://packageinserts.bms.com/pi/pi_opdivo.pdf). Accessed March 3, 2017.
2. Nivolumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at [nccn.org](http://nccn.org). Accessed March 21, 2017.
3. Melanoma (Version 2.2016). In: National Comprehensive Cancer Network Guidelines. Available at [NCCN.org](http://NCCN.org).
4. Non-small cell lung cancer (Version 5.2017). In: National Comprehensive Cancer Network Guidelines. Available at [nccn.org](http://nccn.org).
5. Kidney cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at [NCCN.org](http://NCCN.org).
6. Hodgkin lymphoma (Version 2.2016). In: National Comprehensive Cancer Network Guidelines. Available at [nccn.org](http://nccn.org).
7. Head and neck cancers (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at [nccn.org](http://nccn.org).
8. Bladder cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at [nccn.org](http://nccn.org).

#### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members,** to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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