Kansas City
An Independent Licensee of the Blue Cross and Blue Shield Association

Opdivo (nivolumab)

Policy Number: 5.02.545
Origination: 10/2017
Last Review: 10/2024
Next Review: 10/2025

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for Opdivo when it is determined to be medically necessary because the following criteria have been met.

When Policy Topic is covered

Opdivo is considered **medically necessary** for the following indications:

FDA Approved Indications:

1. **Colorectal cancer, metastatic** (microsatellite instability-high or mismatch repair deficient)
   Treatment (as a single agent or in combination with ipilimumab) of microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer in adults and pediatric patients ≥12 years of age that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
2. **Esophageal carcinoma, squamous cell (unresectable advanced, recurrent, or metastatic)**
   Treatment of unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based chemotherapy.
3. **Head and neck cancer, squamous cell (recurrent or metastatic)**
   Treatment of recurrent or metastatic squamous cell carcinoma of the head and neck in patients with disease progression on or after platinum-based therapy.
4. **Hepatocellular carcinoma**
   Treatment of hepatocellular carcinoma (either as a single agent or in combination with ipilimumab) in patients who have been previously treated with sorafenib.
5. **Hodgkin lymphoma, classical**
   Treatment of classical Hodgkin lymphoma in adult patients who have relapsed or progressed following autologous hematopoietic stem cell transplant (HSCT) and brentuximab vedotin, or after ≥3 lines of systemic therapy that included autologous HSCT.
6. **Malignant pleural mesothelioma, unresectable**
   First-line treatment (in combination with ipilimumab) of unresectable malignant pleural mesothelioma in adults.
7. **Melanoma**
   Adjuvant treatment of melanoma with involvement of lymph nodes or metastatic disease following complete resection.

   Treatment of unresectable or metastatic melanoma (either as a single agent or in combination with ipilimumab).

8. **Non-small cell lung cancer, metastatic**

   First-line treatment of metastatic non-small cell lung cancer (in combination with ipilimumab) in adults whose tumors express PD-L1 (≥1%) as determined by an approved test, and with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.

   First-line treatment of metastatic or recurrent non-small cell lung cancer (in combination with ipilimumab and 2 cycles of platinum doublet chemotherapy) in adults with no EGFR or ALK genomic tumor aberrations.

   Treatment of metastatic non-small cell lung cancer that has progressed on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression (on FDA-approved EGFR- or ALK-directed therapy) prior to receiving nivolumab.

9. **Renal cell cancer, advanced**

   Treatment (as a single agent) of advanced renal cell cancer (RCC) in patients who have received prior anti-angiogenic therapy.

   Treatment of intermediate or poor risk, previously untreated advanced RCC (in combination with ipilimumab).

10. **Small cell lung cancer, metastatic**

    Treatment of metastatic small cell lung cancer in patients with progression after platinum-based chemotherapy and at least one other line of therapy.

11. **Urothelial carcinoma, locally advanced or metastatic**

    Treatment of locally advanced or metastatic urothelial carcinoma in patients with disease progression during or following a platinum-containing therapy or disease progression within 12 months of neoadjuvant or adjuvant treatment with a platinum-containing therapy

Off-Label Uses

1. **Melanoma, metastatic with brain metastases**

   Data (including long-term follow up data) from an open-label, multicenter, phase 2 trial support the use of nivolumab (in combination with ipilimumab) in the treatment of patients with metastatic melanoma and at least one measurable, nonirradiated brain metastasis and no neurologic symptoms (

When Policy Topic is not covered

Opdivo is considered **investigational** in patients less than 18 years of age (except as noted above under colorectal cancer indication) and in patients with all other indications.

Considerations

Opdivo requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

NCDs
https://www.cms.gov/medicare-coverage-database/search-results.aspx?keyword=&keywordType=starts&areaId=s29&docType=NCD&contractOption=all

LCDs
https://www.cms.gov/medicare-coverage-database/search-results.aspx?keyword=&keywordType=starts&areaId=s29&docType=F,P&contractOption=all

Description of Procedure or Service

Background

Opdivo is a monoclonal antibody for the treatment of patients with unresectable (cannot be removed by surgery), metastatic (advanced) melanoma and metastatic non-small cell lung cancer, renal cell carcinoma, relapsed or progressed classical Hodgkin lymphoma, recurrent or metastatic squamous cell carcinoma of the head and neck or locally advanced or metastatic urothelial carcinoma who are no longer responding to other drugs. Opdivo works by inhibiting the PD-1 protein on cell surfaces, which blocks the immune system from attacking melanoma tumors. Opdivo is intended for patients who have been previously treated with ipilimumab and, for melanoma patients whose tumors express a gene mutation called BRAF V600, after treatment with ipilimumab and a BRAF inhibitor have lost effectiveness (1).

Clinically significant immune-mediated adverse reactions may occur with Opdivo therapy including pneumonitis, colitis, hepatitis, nephritis, renal dysfunction, hyperthyroidism, and hypothyroidism. Patients should be monitored for signs and symptoms of adverse reactions and based on the severity, Opdivo should be withheld or discontinued and corticosteroids administered. Opdivo may cause fetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised of the potential hazard to a fetus. Opdivo is administered every 2 weeks until disease progression or unacceptable toxicity (1).

Safety and effectiveness of Opdivo have not been established in pediatric patients younger than 12 years (1).

Warnings and Precautions

- **Adverse reactions (immune mediated):** PD-1/PD-L1 blockers (including nivolumab) remove immune response inhibition, thus potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Severe and fatal immune-mediated adverse reactions may occur in any organ system or tissue. Reactions generally occur during treatment (may occur at any time after nivolumab initiation); reactions may also occur after nivolumab discontinuation. Early identification and management of immune-mediated adverse reactions are necessary to ensure safe use of nivolumab. If suspected immune-mediated reactions occur, initiate appropriate workup to exclude alternative causes (including infection). Medically manage immune-mediated adverse reactions promptly and refer for specialty consultation as appropriate. See "Dosing for Toxicity" for specific instructions.
- **Infusion-related reactions:** Infusion-related reactions have occurred with both single-agent nivolumab and when used in combination with ipilimumab; severe reactions, although rare, were observed.

Rationale

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Opdivo while maintaining optimal therapeutic outcomes.

References

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company. December 2017.

Billing Coding/Physician Documentation Information

J9299	Injection, nivolumab, 1 mg

Additional Policy Key Words

5.02.545

Policy Implementation/Update Information

10/2017	New policy titled Opdivo (nivolumab)
06/2018	New indications added
10/2018	Metastatic small cell lung cancer added to list of approved indications
10/2019	Annual review – no changes made
10/2020	Updated to include all indications
10/2021	Annual review – no changes made
10/2022	Annual review: added off label uses and Warnings and Precautions
10/2023	Annual review: no changes made
10/2024	Annual review: no changes made