BlueCross BlueShield Federal Employee Program

OPDIVO
(nivolumab)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Opdivo (nivolumab) is a monoclonal antibody indicated for the treatment of patients with melanoma, non-small cell lung cancer (NSCLC), malignant pleural mesothelioma, renal cell carcinoma (RCC), hepatocellular carcinoma (HCC), classical Hodgkin lymphoma (cHL), squamous cell carcinoma of the head and neck (SCCHN), urothelial carcinoma, colorectal cancer (CRC), esophageal cancer, gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma. Opdivo works by binding to the programmed cell death-1 (PD-1) receptor, and blocking its interaction with PD-1 ligands, PD-L1 and PD-L2. This interaction releases the inhibitory effects of PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response, resulting in decreased tumor growth (1).

Regulatory Status

FDA-approved indications: Opdivo is a programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of patients with: (1)

1. Melanoma
    a. Unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab
    b. Adjuvant treatment of patients with completely resected Stage IIB, Stage IIC, Stage III, or Stage IV melanoma
2. Non-Small Cell Lung Cancer (NSCLC)
    a. Resectable (tumors ≥4 cm or node positive) NSCLC in the neoadjuvant setting, in combination with platinum-doublet chemotherapy
    b. Resectable (tumors ≥4 cm or node positive) NSCLC and no known EGFR mutations or ALK rearrangements, for neoadjuvant treatment, in combination with platinum-doublet chemotherapy, followed by single-agent Opdivo as adjuvant treatment after surgery
    c. 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, as first-line treatment in combination with ipilimumab
    d. Metastatic or recurrent NSCLC with no EGFR or ALK genomic tumor aberrations as first-line treatment, in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy

e. Metastatic NSCLC and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on an FDA-approved therapy for these aberrations prior to receiving Opdivo

3. Malignant Pleural Mesothelioma
    a. Unresectable malignant pleural mesothelioma, as first-line treatment in combination with ipilimumab
4. Renal Cell Carcinoma (RCC)
    a. Advanced renal cell carcinoma in patients who have received prior anti-angiogenic therapy
    b. First-line treatment of patients with advanced RCC, in combination with cabozantinib
    c. Intermediate or poor risk advanced renal cell carcinoma, as a first-line treatment in combination with ipilimumab
5. Classical Hodgkin Lymphoma (cHL)
    a. Classical Hodgkin lymphoma that has relapsed or progressed after:
        i. Autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin, OR
        ii. 3 or more lines of systemic therapy that includes autologous HSCT
6. Squamous Cell Carcinoma of the Head and Neck (SCCHN)
    a. Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy
7. Urothelial Carcinoma
    a. Adjuvant treatment of patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of UC
    b. Patients with unresectable or metastatic urothelial carcinoma, as first-line treatment in combination with cisplatin and gemcitabine
    c. 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
8. Colorectal Cancer
    a. Unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC) in combination with ipilimumab

   b. Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan

9. Hepatocellular Carcinoma (HCC)
   a. Unresectable or metastatic HCC as a first-line treatment in combination with ipilimumab
   b. Unresectable or metastatic HCC that has been previously treated with sorafenib, in combination with ipilimumab
10. Esophageal Cancer
   a. Completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease, who have received neoadjuvant chemoradiotherapy (CRT)
   b. Unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) as first-line treatment in combination with fluoropyrimidine- and platinum-containing chemotherapy whose tumors express PD-L1 (≥1)
   c. Unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) as first-line treatment in combination with ipilimumab whose tumors express PD-L1 (≥1)
   d. Unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy
11. Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma
   a. Advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma whose tumors express PD-L1 (≥1) in combination with fluoropyrimidine- and platinum-containing chemotherapy

<u>Off-Label Uses</u>: (2)

1. Small cell lung cancer
2. Metastatic anal cancer
3. Merkel cell carcinoma

Opdivo carries warnings for immune-mediated adverse reactions, infusion-related reactions, complications of allogeneic hematopoietic stem cell transplantation (HSCT) and embryo-fetal toxicity. 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 (1).

The safety and effectiveness of Opdivo have not been established in pediatric patients age less than 12 years of age with melanoma or microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC) or in pediatric patients less than 18 years of age for the other approved indications (1).

Summary

Opdivo (nivolumab) is a monoclonal antibody indicated for the treatment of various types of cancers. Opdivo works by binding to the programmed cell death-1 (PD-1) receptor, and blocking its interaction with PD-1 ligands, PD-L1 and PD-L2. This interaction releases the inhibitory effects of PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response, resulting in decreased tumor growth. Opdivo carries warnings for immune-mediated adverse reactions, infusion-related reactions, complications of allogeneic HSCT and embryo-fetal toxicity. The safety and effectiveness of Opdivo have not been established in pediatric patients age less than 12 years of age with melanoma or microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC) or in pediatric patients less than 18 years of age for the other approved indications (1).

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; May 2025.
2. NCCN Drugs & Biologics Compendium® Nivolumab 2025. National Comprehensive Cancer Network, Inc. Accessed on May 7, 2025.