BlueCross BlueShield Federal Employee Program

YERVOY
(ipilimumab)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Yervoy (ipilimumab) is a monoclonal antibody that binds to CTLA-4 (cytotoxic T-lymphocyte antigen 4) and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation, including the activation and proliferation of tumor infiltrating T-effector cells. Inhibition of CTLA-4 signaling can also reduce T-regulatory cell function, which may contribute to a general increase in T-cell responsiveness, including the anti-tumor immune response. The drug is administered intravenously (1-2).

Regulatory Status

FDA-approved indications: Yervoy is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody indicated for: (1)

1. Melanoma
    a. Treatment of unresectable or metastatic melanoma in adults and pediatric patients 12 years and older as a single agent or in combination with nivolumab
    b. Adjuvant treatment of adult patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy
2. Renal Cell Carcinoma (RCC)
    a. Treatment of adult patients with intermediate or poor risk advanced renal cell carcinoma, as first-line treatment in combination with nivolumab
3. Colorectal Cancer
    a. Treatment of adult and pediatric patients 12 years of age and older with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC) in combination with nivolumab
4. Hepatocellular Carcinoma (HCC)
    a. Adult patients with unresectable or metastatic HCC as first-line treatment in combination with nivolumab
    b. In combination with nivolumab in adult patients with unresectable or metastatic HCC who have been previously treated with sorafenib
5. Non-Small Cell Lung Cancer (NSCLC)

   a. Treatment of adult patients with metastatic non-small cell lung cancer expressing 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 nivolumab
   b. Treatment of adult patients with metastatic or recurrent NSCLC with no EGFR or ALK genomic tumor aberrations as first-line treatment, in combination with nivolumab and 2 cycles of platinum-doublet chemotherapy
6. Malignant Pleural Mesothelioma
   a. Treatment of adult patients with unresectable malignant pleural mesothelioma, as first-line treatment in combination with nivolumab
7. Esophageal squamous cell carcinoma
   a. Treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma, as first-line treatment in combination with nivolumab whose tumors express PD-L1 (≥1)

Off-Label Uses: (2)

1. Retreatment of melanoma in patients who experience disease control but who relapse or progress greater than 3 months after treatment discontinuation
2. Central nervous system (CNS) metastases if active against primary tumor (melanoma)
3. Small cell lung cancer (SCLC) in combination with nivolumab

Yervoy has a warning regarding severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated adverse reactions include colitis, hepatitis, dermatitis (including toxic epidermal necrolysis), endocrinopathies, pneumonitis, and nephritis. The majority of these immune-mediated reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuation of ipilimumab.Permanently discontinue Yervoy and initiate systemic high-dose corticosteroid therapy for severe immune-mediated reactions. Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy and evaluate clinical chemistries including liver function tests, adrenocorticotropic hormone (ACTH) level, and thyroid function tests at baseline and before each dose (1).

Yervoy is only given for 4 doses with nivolumab for renal cell carcinoma, colorectal cancer, and hepatocellular carcinoma. After that, nivolumab is given as a single agent (1).

Yervoy is only given for up to 2 years for patients with NSCLC and malignant pleural mesothelioma. Yervoy is only given for up to 3 years for patients for the adjuvant treatment of melanoma (1).

Safety and effectiveness of Yervoy for pediatric patients less than 12 years of age have not been established (1).

Summary

Yervoy (ipilimumab) is a monoclonal antibody that binds to CTLA-4 (cytotoxic T-lymphocyte antigen 4) and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation, including the activation and proliferation of tumor infiltrating T-effector cells. The most common severe immune-mediated adverse reactions include colitis, hepatitis, dermatitis (including toxic epidermal necrolysis), endocrinopathies, \pneumonitis, and nephritis (1-2).

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

References

1. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2025.
2. NCCN Drugs & Biologics Compendium® Ipilimumab 2025. National Comprehensive Cancer Network, Inc. Accessed on May 7, 2025