Yervoy (ipilimumab)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Yervoy (ipilimumab) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. Yervoy (ipilimumab) is a recombinant, human monoclonal antibody that binds to the cytotoxic T-lymphocyte-associated antigen 4 (CTLA-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.

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Unresectable or Metastatic Melanoma
   a) Yervoy is indicated for the treatment of unresectable or metastatic melanoma in adults and pediatric patients (12 years and older).
   b) Yervoy, in combination with nivolumab, is indicated for the treatment of unresectable or metastatic melanoma in adult patients.

2. Adjuvant Treatment of Melanoma
   Yervoy is indicated for the adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy.

3. Advanced Renal Cell Carcinoma
   Yervoy, in combination with nivolumab, is indicated for the first-line treatment of patients with intermediate or poor risk advanced renal cell carcinoma (RCC).

4. Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Metastatic Colorectal Cancer
   Yervoy, in combination with nivolumab, is indicated for the treatment of adult and pediatric patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

5. Hepatocellular Carcinoma
   Yervoy, in combination with nivolumab, is indicated for the treatment of patients with hepatocellular carcinoma who have been previously treated with sorafenib.

6. Metastatic Non-small Cell Lung Cancer
   a. Yervoy, in combination with nivolumab, is indicated for the first-line treatment of adult patients with 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.
   b. Yervoy, in combination with nivolumab and 2 cycles of platinum-doublet chemotherapy, is indicated for the first-line treatment of adult patients with metastatic or recurrent non-small cell lung cancer with no EGFR or ALK genomic tumor aberrations.

7. Malignant Pleural Mesothelioma
   Yervoy, in combination with nivolumab, is indicated for the first-line treatment of adult patients with unresectable malignant pleural mesothelioma, as first-line treatment.
8. Esophageal Cancer
   Yervoy, in combination with nivolumab, is indicated fo the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).

Compendial Uses
1. Cutaneous melanoma
2. Uveal melanoma
3. Central nervous system (CNS) brain metastases
4. Non-small cell lung cancer
5. Renal Cell Carcinoma
6. Colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma
7. Malignant pleural mesothelioma
8. Malignant peritoneal mesothelioma
9. Hepatocellular Carcinoma
10. Small bowel adenocarcinoma
11. Ampullary adenocarcinoma

POLICY

Required Documentation
Submission of the following information is necessary to initiate the prior authorization review:

A. Documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.
B. Documentation of molecular testing for EGFR exon 19 deletions or L858R mutations and ALK rearrangements, where applicable.

Criteria for Initial Approval

A. Cutaneous Melanoma
Authorization of 6 months may be granted for treatment of cutaneous melanoma when any of the following conditions are met:
1. Yervoy will be used as a single agent or in combination with nivolumab (for a maximum of 4 doses) for metastatic or unresectable disease.
2. Yervoy will be used as a single agent (up to 3 years) as adjuvant treatment of stage III or IV disease following complete resection or no evidence of disease.

3. Yervoy will be used as subsequent therapy in combination with pembrolizumab for metastatic or unresectable disease in members who progressed on single-agent anti-programmed death 1 (PD-1) immunotherapy.
4. Yervoy will be used as a single agent for limited resectable local recurrence after prior anti-PD-1 therapy

B. Uveal Melanoma
Authorization of 6 months may be granted as a single agent or in combination with nivolumab for treatment of uveal melanoma for distant metastatic disease.

C. CNS Brain Metastases
Authorization of 6 months may be granted as a single agent or in combination with nivolumab for treatment of CNS brain metastases in members with melanoma.

D. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted for treatment of recurrent, advanced or metastatic non-small cell lung cancer if there are no EGFR exon 19 deletions or L858R mutations or ALK rearrangements (unless testing is not feasible due to insufficient tissue) and the requested medication will be used in a regimen containing nivolumab.

E. Renal Cell Carcinoma
Authorization of 6 months may be granted for treatment of renal cell carcinoma, in combination with nivolumab (for 4 cycles, followed by single agent nivolumab) for relapsed, advanced, or stage IV disease, in any of the following settings:
1. First-line therapy for poor or intermediate risk.
2. First-line therapy for clear cell histology and favorable risk.
3. Subsequent therapy for clear cell histology.

F. Colorectal Cancer
Authorization of 6 months may be granted for treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, for microsatellite instability-high or mismatch repair deficient tumors when used in combination with nivolumab (for a maximum of 4 doses) for advanced, metastatic, unresectable, or inoperable disease.

G. Malignant Pleural or Peritoneal Mesothelioma
Authorization of 6 months may be granted in combination with nivolumab for treatment of malignant pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma.

H. Hepatocellular Carcinoma
Authorization of 6 months may be granted in combination with nivolumab (for a maximum of 4 doses) for subsequent treatment of hepatocellular carcinoma.

I. Small Bowel Adenocarcinoma
Authorization of 6 months may be granted in combination with nivolumab for treatment of advanced or metastatic small bowel adenocarcinoma for microsatellite instability-high or mismatch repair deficient tumors.

J. **Ampullary Adenocarcinoma**
Authorization of 6 months may be granted in combination with nivolumab for treatment of progressive unresectable, or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) ampullary adenocarcinoma.

K. Esophageal Cancer
Authorization of 6 months may be granted in combination with nivolumab for the first-line treatment of unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).

Continuation of Therapy

A. Adjuvant Treatment of Melanoma
Authorization of 6 months may be granted (up to 3 years) for continued treatment in members requesting reauthorization for adjuvant melanoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

B. Cutaneous Melanoma, Renal Cell Carcinoma, Colorectal Cancer, Hepatocellular Cancer
Authorization of 6 months may be granted (up to 4 doses maximum, if member has not already received 4 doses) for continued treatment in members requesting reauthorization for cutaneous melanoma, renal cell carcinoma, colorectal cancer, and hepatocellular cancer when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

C. Non-Small Cell Lung Cancer, Esophageal Cancer, or Malignant Pleural or Peritoneal Mesothelioma
Authorization of 6 months may be granted (up to 24 months total) for continued treatment in members requesting reauthorization for non-small cell lung cancer, esophageal cancer, or malignant pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma subtypes, when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

D. All Other Indications
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for all other indications listed in Criteria for Initial Approval Section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Yervoy is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J9228 Injection, ipilimumab, 1mg

REFERENCES

- Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2022.
- The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 18, 2022.

POLICY HISTORY

Policy #: 05.02.23
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