Reference number(s)
1796-A

SPECIALTY GUIDELINE MANAGEMENT

YERVOY (ipilimumab)

POLICY

I. INDICATIONS

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.

A. FDA-Approved Indications

1. Unresectable or Metastatic Melanoma
   Yervoy is indicated for the treatment of unresectable or metastatic melanoma in adults and pediatric patients (12 years and older).

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 treatment of patients with intermediate or poor risk, previously untreated 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 is indicated for the treatment of hepatocellular carcinoma in combination with nivolumab, in patients who have been previously treated with sorafenib.

6. Non-small Cell Lung Cancer
   Yervoy is indicated for the 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.

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

7. Malignant Pleural Mesothelioma
   Yervoy, in combination with nivolumab, is indicated for the treatment of adult patients with unresectable malignant pleural mesothelioma, as first-line treatment.

B. 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 carcinoma and anal adenocarcinoma
7. Malignant pleural mesothelioma
8. Hepatocellular Carcinoma
9. Small bowel adenocarcinoma, including advanced ampullary cancer

All other indications are considered experimental/investigational and not medically necessary.

II. 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

III. 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 in combination with pembrolizumab for metastatic or unresectable disease in members who progressed on single-agent anti-programmed death 1 (PD-1) immunotherapy.

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 carcinoma 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 Mesothelioma

Authorization of 6 months may be granted in combination with nivolumab for treatment of malignant pleural 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, including advanced ampullary cancer, for microsatellite-instability high or mismatch repair deficient tumors.

IV. 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 or Malignant Pleural 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 or malignant pleural mesothelioma 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 Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; November 2020.
2. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed January 19, 2022.
3. Danielli R, Ridolfi R, Chiarion-Sileni V, et al. Ipilimumab in pretreated patients with metastatic uveal melanoma: Safety and clinical efficacy. Cancer Immunol Immunother. 2012;61(1):41-48.
4. Piulats JM, Cruz-Merino LDL, Garcia MTC, et al. Phase II multicenter, single arm, open label study of nivolumab (NIVO) in combination with ipilimumab (IPI) as first line in adult patients (pts) with metastatic uveal melanoma (MUM): GEM1402 NCT02626962 (abstract). J Clin Oncol 2017;35:Abstr 9533.