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 as a single agent or in combination with nivolumab for the treatment of unresectable or metastatic melanoma in adult and pediatric patients 12 years and older.

2. Adjuvant Treatment of Melanoma
   Yervoy is indicated for the 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.

3. Advanced Renal Cell Carcinoma
   Yervoy, in combination with nivolumab, is indicated for the first-line treatment of adult 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 adult 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.

8. Esophageal Cancer

Yervoy, in combination with nivolumab, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).

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 adenocarcinoma and anal adenocarcinoma
7. Malignant pleural mesothelioma
8. Malignant peritoneal mesothelioma
9. Hepatocellular carcinoma
10. Small bowel adenocarcinoma
11. Ampullary adenocarcinoma
12. Esophageal/Esophagogastric Junction Cancers
13. Kaposi Sarcoma
14. Bone Cancer
15. Biliary Tract Cancers
    a. Cholangiocarcinoma
    b. Gallbladder Cancer
16. Soft Tissue Sarcoma
    a. Extremity/body wall sarcoma
    b. Head/neck sarcoma
    c. Retroperitoneal/intra-abdominal sarcoma
    d. Rhabdomyosarcoma
    e. Angiosarcoma
17. Merkel Cell Carcinoma

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 exon 21 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 in any of the following settings:
1. The requested medication will be used as a single agent or in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) for progressive, metastatic or unresectable disease.
2. The requested medication will be used as a single agent or in combination with nivolumab as adjuvant treatment of stage III or IV disease if no evidence of disease following metastasis-directed therapy (i.e., complete resection).

3. The requested medication will be used as subsequent therapy at a low dose in combination with pembrolizumab, or nivolumab for metastatic or unresectable disease in members who progressed on single-agent anti-programmed death 1 (PD-1) immunotherapy or BRAF-targeted therapy.
4. The requested medication 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 exon 21 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 4doses, followed by single agent nivolumab) for relapsed, advanced, or stage IV disease with clear cell histology as:
1. First-line therapy for poor or intermediate risk.
2. First-line therapy for favorable risk.
3. Subsequent therapy.

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 (MSI-H) or mismatch repair deficient (dMMR) tumors when used in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) 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 as a single agent or in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) for 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 (MSI-H) or mismatch repair deficient (dMMR) 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 and Esophagogastric Junction Cancers
Authorization of 6 months may be granted in combination with nivolumab for the first-line treatment of unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC).

L. Kaposi Sarcoma
Authorization of 6 months may be granted in combination with nivolumab for subsequent treatment of relapsed/refractory classic Kaposi Sarcoma.

M. Bone Cancer
Authorization of 6 months may be granted in combination with nivolumab for unresectable or metastatic disease when all of the following are met:
1. Disease has tumor mutation burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] tumors
2. Disease has progressed following prior treatment and has no satisfactory alternative treatment options

N. Biliary Tract Cancer (Cholangiocarcinoma and Gallbladder Cancer)
Authorization of 6 months may be granted as subsequent treatment in combination with nivolumab for unresectable or resected gross residual (R2) disease, progressive or metastatic disease that is tumor mutation burden-high (TMB-H).

O. Soft Tissue Sarcoma
Authorization of 6 months may be granted in combination with nivolumab for treatment of extremity/body wall sarcomas, head/neck sarcomas and retroperitoneal/intra-abdominal sarcomas, rhabdomyosarcoma and angiosarcoma.

P. Merkel Cell Carcinoma
Authorization of 6 months may be granted in combination with nivolumab for treatment of progressive, unresectable, recurrent, or stage IV Merkel cell carcinoma.

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 treatment guidelines do not specify a limited number of total doses (see above) and there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

C. Non-Small Cell Lung Cancer, Esophageal/Esophagogastric Junction Cancers, 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, esophageal cancer, or malignant pleural 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 Section III when treatment guidelines do not specify a limited number of total doses (see above) and 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; February 2023.
2. The NCCN Drugs & Biologics Compendium 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 8, 2023.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Anal Carcinoma. Version 3.2022. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf Accessed March 8, 2023.
4. Lexicomp [database online]. Hudson, OH: Lexi-Comp, Inc.; https://online.lexi.com/lco/action/home [available with subscription]. Accessed March 13, 2023.