| Reference number(s) |
| --- |
| 1796-A |

# Specialty Guideline Management
# Yervoy

## Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

| Brand Name | Generic Name |
| --- | --- |
| Yervoy | Iplilimumab |

## 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.

### 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.

#### 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.

#### 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).

### 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 unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC).

### Hepatocellular Carcinoma

- Yervoy, in combination with nivolumab, is indicated for the first-line treatment of adult patients with unresectable or metastatic hepatocellular carcinoma (HCC).
- Yervoy, in combination with nivolumab, is indicated for the treatment of adult patients with unresectable or metastatic HCC who have been previously treated with sorafenib.

### Metastatic Non-small Cell Lung Cancer

- 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.
- 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.

### Malignant Pleural Mesothelioma

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

### 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) whose tumors express PD-L1 (≥1 ).

## Compendial Uses[2]

- Cutaneous melanoma
- Uveal melanoma
- Gestational trophoblastic neoplasia
- Central nervous system (CNS) brain metastases
- Non-small cell lung cancer
- Renal cell carcinoma
- Colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma
- Pleural mesothelioma
- Peritoneal mesothelioma
- Hepatocellular carcinoma

- Small bowel adenocarcinoma
- Ampullary adenocarcinoma
- Esophageal/Esophagogastric Junction Cancers
- Kaposi Sarcoma
- Bone Cancer
- Biliary Tract Cancers
  - Cholangiocarcinoma
  - Gallbladder Cancer
- Soft Tissue Sarcoma
  - Extremity/body wall sarcoma
  - Head/neck sarcoma
  - Retroperitoneal/intra-abdominal sarcoma
  - Rhabdomyosarcoma
  - Angiosarcoma
- Merkel Cell Carcinoma
- Gastric Cancer

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

# Documentation

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

- Documentation of laboratory report confirming MSI-H, mismatch repair deficient (dMMR), or polymerase epsilon/delta (POLE/POLD1) tumor status, where applicable.
- Documentation of molecular testing for EGFR alterations and ALK, RET, and ROS1 rearrangements, where applicable.

# Coverage Criteria

## Cutaneous Melanoma[1,2]

Authorization of 6 months may be granted for treatment of cutaneous melanoma in any of the following settings:

- The requested medication will be used as a single agent (for up to 4 doses) or in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) for metastatic or unresectable disease.
- The requested medication will be used as a single agent (for up to 8 doses) or in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) as adjuvant treatment if no evidence of disease following systemic or metastasis-directed therapy (e.g., complete resection).

- The requested medication will be used at a low dose in combination with pembrolizumab for disease progression following anti-PD-1 therapy as subsequent therapy for metastatic or unresectable disease.
- The requested medication will be used as a single agent (for up to 8 doses) for resectable disease after prior anti-PD-1 therapy.
- The requested medication will be used in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) as neoadjuvant treatment.

## Uveal Melanoma[2]

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 uveal melanoma for unresectable or metastatic disease.

## Gestational Trophoblastic Neoplasia[2]

Authorization of 6 months may be granted in combination with nivolumab for treatment of gestational trophoblastic neoplasia for multiagent chemotherapy-resistant disease when either of the following criteria is met:

- Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor).
- Member has high-risk disease.

## CNS Brain Metastases[2]

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 CNS brain metastases in members with melanoma.

## Non-Small Cell Lung Cancer (NSCLC)[1,2]

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, RET, or ROS1 rearrangements (unless testing is not feasible due to insufficient tissue) and the requested medication will be used in a regimen containing nivolumab.

## Renal Cell Carcinoma[1,2]

Authorization of 6 months may be granted for treatment of renal cell carcinoma in combination with nivolumab (for 4 doses, followed by single agent nivolumab) for relapsed, advanced, or stage IV disease with clear cell histology.

## Colorectal Cancer[1,2,3]

Authorization of 6 months may be granted for treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, for microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR) or polymerase epsilon/delta (POLE/POLD1) tumors with ultra-hypermutated phenotype (e.g., tumor mutational burden (TMB) > 50 mut/Mb) when used in combination with nivolumab (for 4 doses followed by nivolumab as a single agent).

## Pleural or Peritoneal Mesothelioma[1,2]

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

## Hepatocellular Carcinoma[1,2]

Authorization of 6 months may be granted for treatment of hepatocellular carcinoma in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) for either of the following:

- First-line treatment of unresectable or extrahepatic/metastatic disease
- Subsequent treatment

## Small Bowel Adenocarcinoma[2]

Authorization of 6 months may be granted in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) for treatment of unresectable, medically inoperable, advanced or metastatic small bowel adenocarcinoma for microsatellite-instability high (MSI-H), mismatch repair deficient (dMMR) or polymerase epsilon/delta (POLE/POLD1) tumors with ultra-hypermutated phenotype (e.g., tumor mutational burden (TMB) > 50 mut/Mb).

## Ampullary Adenocarcinoma[2]

Authorization of 6 months may be granted in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) for treatment of progressive or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) ampullary adenocarcinoma.

## Esophageal and Esophagogastric Junction Cancers[1,2]

- Authorization of 6 months may be granted in combination with nivolumab for the treatment of esophageal or esophagogastric junction cancer in members who are not surgical candidates or have unresectable locally advanced, recurrent or metastatic disease and PD-L1 ≥ 1.
- Authorization of 6 months may be granted in combination with nivolumab for treatment of esophageal or esophagogastric junction adenocarcinoma if tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).

- Authorization of 6 months may be granted for induction therapy for relieving dysphagia in combination with nivolumab for members with PD-L1 ≥ 1 planned for esophagectomy.

## Gastric Cancer[2,5]

Authorization of 6 months may be granted in combination with nivolumab for treatment of gastric adenocarcinoma if tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).

## Kaposi Sarcoma[2]

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

## Bone Cancer[2]

Authorization of 6 months may be granted in combination with nivolumab for unresectable or metastatic disease when all of the following are met:

- Disease has tumor mutation burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] tumors
- Disease has progressed following prior treatment and has no satisfactory alternative treatment options

## Biliary Tract Cancer (Cholangiocarcinoma and Gallbladder Cancer)[2]

Authorization of 6 months may be granted in combination with nivolumab for subsequent treatment of unresectable or resected gross residual (R2) disease, or metastatic disease that is tumor mutation burden-high (TMB-H).

Authorization of 6 months may be granted in combination with nivolumab for neoadjuvant treatment of resectable locoregionally advanced gallbladder cancer that is tumor mutation burden-high (TMB-H) when disease does not present as jaundice.

## Soft Tissue Sarcoma[2]

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.

## Merkel Cell Carcinoma[2,4]

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 primary node positive regional, unresectable, recurrent, or stage IV Merkel cell carcinoma.

# Continuation of Therapy

## 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.

## 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.

## Non-Small Cell Lung Cancer, Gastric/ Esophageal/Esophagogastric Junction Cancers, or 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 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.

## Biliary Tract Cancer

Authorization of 6 months may be granted (for 2 to 6 months total for neoadjuvant treatment, and for up 24 months total for other clinical settings) for continued treatment in members requesting reauthorization for biliary tract cancer when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

## All Other Indications

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for all other indications listed in the Coverage Criteria section 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.

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# References


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