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	ipilimumab

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 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]

- Adrenal Gland Tumors
- Ampullary adenocarcinoma
- Appendiceal neoplasms and cancers
- Biliary Tract Cancers
  - Cholangiocarcinoma
  - Gallbladder Cancer
- Bone Cancer
- Central nervous system (CNS) brain metastases
- Cervical Cancer
- Colorectal cancer, including anal adenocarcinoma
- Cutaneous melanoma

- Esophageal/Esophagogastric Junction Cancers
- Gastric Cancer
- Gestational trophoblastic neoplasia
- Hepatocellular carcinoma
- Kaposi Sarcoma
- Merkel Cell Carcinoma
- Non-small cell lung cancer
- Peritoneal mesothelioma
- Pleural mesothelioma
- Renal cell carcinoma
- Small bowel adenocarcinoma
- Soft Tissue Sarcoma
  - Angiosarcoma
  - Dedifferentiated liposarcoma
  - Epithelioid hemangioendothelioma
  - Extremity/body wall sarcoma
  - Head/neck sarcoma
  - Retroperitoneal/intra-abdominal sarcoma
  - Rhabdomyosarcoma
- Uterine Neoplasms
  - Endometrial Carcinoma
  - Uterine Sarcoma
- Uveal Melanoma
- Vaginal Cancer
- Vulvar 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 microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or polymerase epsilon/delta (POLE/POLD1) tumor status, where applicable.
- Documentation of the absence of EGFR exon 19 deletion and exon 21 L858R mutations, ALK, RET, and ROS1 gene fusions, where applicable.

Coverage Criteria

Adrenal Gland Tumors

Authorization of 6 months may be granted in combination with nivolumab for treatment of unresectable or metastatic adrenocortical carcinoma.

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.

Appendiceal Neoplasms and Cancers[2,6]

Authorization of 6 months may be granted for treatment of appendiceal neoplasms and appendiceal cancers (including appendiceal adenocarcinoma, goblet cell adenocarcinoma, and undifferentiated carcinoma not otherwise specified) 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).

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 gross residual (R2), or metastatic extrahepatic or intrahepatic cholangiocarcinoma or gallbladder cancer that is tumor mutational 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 mutational burden-high (TMB-H) when disease does not present as jaundice.

Bone Cancer[2]

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

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

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 BRAF non-specific melanoma.

Cervical Cancer[2]

Authorization of 6 months may be granted in combination with nivolumab for subsequent treatment of cervical cancer when either of the following criteria is met:

- Disease is recurrent or metastatic.
- Disease is persistent small cell neuroendocrine carcinoma of the cervix (NECC).

Colorectal Cancer[1-3]

Authorization of 6 months may be granted for treatment of colorectal cancer, including 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).

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.

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 for either of the following:

- First-line therapy when PD-L1 ≥ 1.
- Subsequent therapy.

Authorization of 6 months may be granted in combination with nivolumab for treatment of esophageal or esophagogastric junction cancer 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 esophageal or esophagogastric junction squamous cell carcinoma 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).

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.

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.

Kaposi Sarcoma[2]

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

Merkel Cell Carcinoma[2,4]

Authorization of 6 months may be granted as a single agent or in combination with nivolumab for treatment of regional, in-transit, unresectable, recurrent, or stage IV Merkel cell carcinoma.

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 gene fusions (unless testing is not feasible due to insufficient tissue) and the requested medication will be used in a regimen containing nivolumab.

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.

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.

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).

Soft Tissue Sarcoma[2]

Authorization of 6 months may be granted in combination with nivolumab for treatment of rhabdomyosarcoma and epithelioid hemangioendothelioma that is tumor mutational burden-high (TMB-H) [≥10 mut/Mb].

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

Uterine Neoplasms[2]

Authorization of 6 months may be granted in combination with nivolumab for subsequent treatment of recurrent unresectable or metastatic endometrial carcinoma that is tumor mutational burden-high (TMB-H) [≥10 mut/Mb] and has no satisfactory alternative treatment options.

Authorization of 6 months may be granted in combination with nivolumab for subsequent treatment of unresectable or metastatic uterine sarcoma that is tumor mutational burden-high (TMB-H) [≥10 mut/Mb] and has no satisfactory alternative treatment options.

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.

Vaginal Cancer[2]

Authorization of 6 months may be granted as subsequent therapy for recurrent or metastatic vaginal cancer when used in combination with nivolumab.

Vulvar Cancer[2]

Authorization of 6 months may be granted as subsequent therapy for advanced or recurrent/metastatic vulvar cancer when used in combination with nivolumab.

Continuation of Therapy

Biliary Tract Cancer

Authorization of 6 months may be granted (for 2 to 6 months total for neoadjuvant treatment, and for up to 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.

Cervical Cancer, Esophageal/Esophagogastric Junction Cancers, Non-Small Cell Lung Cancer, Pleural or Peritoneal Mesothelioma

Authorization of 6 months may be granted (up to 24 months total) for continued treatment in members requesting reauthorization for cervical cancer, non-small cell lung cancer, esophageal/esophagogastric junction cancer, or 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.

Cutaneous Melanoma, Colorectal Cancer, Hepatocellular Cancer, Renal Cell Carcinoma

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, colorectal cancer, hepatocellular cancer, and renal cell carcinoma 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.

References

1. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2025.
2. The NCCN Drugs & Biologics Compendium ® © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed December 2, 2025.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Anal Carcinoma. Version 5.2025. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf Accessed December 2, 2025.
4. Lexicomp Online, Lexi-Drugs Online. Waltham, MA: UpToDate, Inc.; 2025 http://online.lexi.com. Accessed December 2, 2025.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Gastric Cancer Version 3.2025. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf Accessed December 2, 2025.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Appendiceal Neoplasms and Cancers Version 1.2026. https://www.nccn.org/professionals/physician_gls/pdf/appendiceal.pdf Accessed December 30, 2025.