Clinical Policy: Ipilimumab (Yervoy)

Reference Number: PA.CP.PHAR.319
Effective Date: 01/2018
Last Review Date: 04/2026

Description
Ipilimumab (Yervoy®) is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody.

FDA Approved Indication(s)
Yervoy is indicated for:

- **Melanoma**
  - Treatment of unresectable or metastatic melanoma in adults and pediatric patients 12 years and older as a single agent or in combination with nivolumab
  - Aduvant 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
- **Renal cell carcinoma (RCC)**
  - Treatment of adult patients with intermediate or poor risk, advanced renal cell carcinoma, as first-line treatment in combination with nivolumab
- **Colorectal cancer (CRC)**
  - Treatment of adult and pediatric patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) unresectable or metastatic CRC in combination with nivolumab
- **Hepatocellular carcinoma (HCC)**
  - Treatment of adult patients with unresectable or metastatic HCC, as first-line treatment in combination with nivolumab
  - In combination with nivolumab in adult patients with unresectable or metastatic HCC who have been previously treated with sorafenib
- **Non-small cell lung cancer (NSCLC)**
  - In combination with nivolumab, for the first-line treatment of adult patients with metastatic NSCLC whose tumors express programmed death-ligand 1 (PD-L1) ≥ 1% as determined by an FDA-approved test, with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations
  - In combination with nivolumab and 2 cycles of platinum-doublet chemotherapy, for the first-line treatment of adult patients with metastatic or recurrent NSCLC, with no EGFR or ALK genomic tumor aberrations
- **Malignant pleural mesothelioma**
  - Treatment of adult patients with unresectable malignant pleural mesothelioma, as first-line treatment in combination with nivolumab.
- **Esophageal cancer**
  - Treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC), as first line treatment in combination with nivolumab whose tumors express PD-L1 (≥1)

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness ® that Yervoy is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Melanoma (must meet all):
1. Diagnosis of melanoma and disease meets one of the following (a, b, c or d):
   a. Unresectable or metastatic;
   b. Resectable, limited resectable, or lymph node positive;
   c. Recurrent;
   d. Other NCCN recommendations listed as category 1, 2A, or 2B;
2. Prescribed by or in consultation with an oncologist;
3. Age is one of the following (a or b):
   a. For unresectable or metastatic disease: ≥ 12 years;
   b. For adjuvant or neoadjuvant treatment: ≥ 18 years;
4. Prescribed in one of the following ways (a, b or c):
   a. As a single agent;
   b. In combination with Opdivo®*;
   c. In combination with Keytruda® or Imlygic* for unresectable or metastatic melanoma;
   **Prior authorization may be required for Opdivo, Imlygic and Keytruda*
5. Request meets one of the following (a, b, or c):*
   a. Unresectable or metastatic disease: Dose does not exceed 3 mg per kg every 3 weeks for a maximum of 4 doses;
   b. Adjuvant treatment: Dose does not exceed 3 mg/kg every 3 weeks for 4 doses, followed by 3 mg/kg every 12 weeks for up to 4 additional doses;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

Approval duration: 12 months

B. Renal Cell Carcinoma (must meet all):
1. Diagnosis of relapsed, advanced or metastatic renal cell carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Prescribed in combination with Opdivo®;
   **Prior authorization may be required for Opdivo*
5. Request meets one of the following (a or b):
   a. Dose does not exceed 1 mg/kg IV every 3 weeks for a maximum of 4 doses;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

Approval duration: 16 weeks (maximum of 4 doses)

C. Colorectal Cancer (must meet all)**:**
1. Diagnosis of colorectal cancer with one of the following mutations (a, b or c):
   a. MSI-H;
   b. dMMR;
   c. Polymerase epsilon/delta (POLE/POLD1);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. One of the following (a or b):
   a. Disease is advanced, progressive, unresectable or metastatic;
   b. Other NCCN recommendations listed as category 1, 2A, or 2B;
5. Prescribed in combination with Opdivo;
   **Prior authorization may be required for Opdivo*
6. Request meets one of the following (a or b):
   a. Dose does not exceed 1 mg/kg IV every 3 weeks for a maximum of 4 doses;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 16 weeks (maximum of 4 doses)

D. Hepatocellular Cancer (HCC) (must meet all)**:**
1. Diagnosis of HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Prescribed in combination with nivolumab (Opdivo);
   **Prior authorization may be required for Opdivo*
5. Documentation of Child-Pugh Class A status;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 3 mg/kg IV every 3 weeks for a maximum of 4 doses;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 16 weeks (maximum of 4 doses)

E. Non-Small Cell Lung Cancer (must meet all)**:**
1. Diagnosis of recurrent, advanced or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with Opdivo;
   **Prior authorization may be required for Opdivo*
5. Member does not have contraindication to PD-1/PD-L1 inhibitor therapy (e.g., Opdivo, Keytruda, Tecentriq, Imfinzi) (*see Appendix D*);
6. Request meets one of the following (a-d):*
   a. Disease mutation status is negative for actionable biomarkers (EGFR, KRAS, ALK, ROS1, NRG1, BRAF, NTRK1/2/3, MET, RET and ERBB2 [HER2]);
   b. Disease mutation status is positive for EGFR S768I, L861Q, and/or G719X, and member has received prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib;

c. Disease mutation status is positive for EGFR exon 20, KRAS G12C, NRTK1/2/3, BRAF V600E, MET exon 14 skipping, NRG1 gene fusion, or ERBB2 (HER2);
d. Other NCCN recommendations listed as category 1, 2A, or 2B;

**Prior authorization may be required*

7. Request meets one of the following (a or b):
   a. Dose does not exceed 1 mg/kg IV every 6 weeks in combination with Opdivo;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 12 months

F. Malignant Pleural Mesothelioma (must meet all)**:**

1. Diagnosis of malignant pleural mesothelioma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with Opdivo;*

   **Prior authorization may be required for Opdivo.*
5. Request meets one of the following (a or b):
   a. Dose does not exceed 1 mg/kg IV every 6 weeks in combination with Opdivo;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

G. Esophageal Cancer (must meet all)**:**

1. Diagnosis ESCC and one of the following (a or b):
   a. Tumor expresses PD-L1(Combined Positive Score [CPS] ≥ 1) and one of the following (i or ii);
      i. Disease is unresectable advanced, recurrent or metastatic;
      ii. Prescribed as induction or palliative therapy;
   b. Tumor is characterized as MSI-H or dMMR and one of the following (i or ii);
      i. Prescribed as induction, neoadjuvant, perioperative, or palliative therapy (*off-label*);
      ii. Disease is unresectable locally advanced, recurrent, or metastatic;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with Opdivo;*

   **Prior authorization may be required for Opdivo.*
5. Request meets one of the following (a or b):
   a. Dose does not exceed 1 mg/kg IV every 6 weeks in combination with Opdivo;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

H. NCCN Compendium Indications (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a-p):
   a. One of the following MSI-H or dMMR tumor cancers (i-v):
      i. Ampullary adenocarcinoma;

ii. Appendiceal neoplasms and cancers;
iii. Esophageal adenocarcinoma;
iv. Gastric cancer;
v. Small bowel adenocarcinoma;

b. One of the following POLE/POLD mutation with ultra-hypermutated phenotype (e.g., TMB > 50 mutations/megabase) tumor cancers (i or ii):
i. Appendiceal neoplasms and cancers;
ii. Small bowel adenocarcinoma;

c. Bone cancer (e.g., chondrosarcoma, osteosarcoma, chordoma, Ewing sarcoma), and both of the following (i and ii):
i. Disease is unresectable or metastatic with tissue tumor mutation burden-high tumors with 10 or more mutations per megabase;
ii. Disease has progressed following prior treatment and no satisfactory alternative treatment options exist;

d. BRAF non-specific melanoma brain metastases;
e. Biliary tract cancer (e.g., gallbladder, intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma);
f. Cervical cancer as subsequent therapy;
g. Gestational trophoblastic neoplasia;
h. Classic Kaposi sarcoma as subsequent systemic therapy;
i. Metastatic or unresectable uveal melanoma;
j. Merkel cell carcinoma;
k. Metastatic, locally advanced, or unresectable neuroendocrine and adrenal tumors;
l. Soft tissue sarcoma and one of the following (i or ii):
i. Disease is angiosarcoma;
ii. Prescribed as subsequent therapy for advanced, unresectable or metastatic disease, and disease is one of the following (1-6):
1. Tumor mutation burden-high (≥ 10 mutations per megabase);
2. Myxofibrosarcoma;
3. Undifferentiated pleomorphic sarcoma;
4. Dedifferentiated liposarcoma;
5. Cutaneous angiosarcoma;
6. Undifferentiated sarcomas;

m. Uterine neoplasms (e.g. endometrial carcinoma, uterine sarcoma) as subsequent therapy, and both of the following (i and ii):;
i. Disease is unresectable or metastatic with tumor mutation burden-high tumors (≥ 10 mutations per megabase);
ii. Disease has progressed following prior treatment and no satisfactory alternative treatment options exist;

n. Vaginal cancer as subsequent therapy;
o. Vulvar cancer as subsequent therapy;
p. Other NCCN recommendations listed as category 1, 2A, or 2B;

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Prescribed in combination with Opdivo for all of the following (a-k):*
a. One of the following MSI-H or dMMR tumor cancers (i-v):

i. Ampullary adenocarcinoma;
ii. Appendiceal neoplasms and cancers;
iii. Esophageal adenocarcinoma
iv. Gastric cancer;
v. Small bowel adenocarcinoma;

b. Bone cancer;
c. Biliary tract cancer;
d. Cervical cancer;
e. Classic Kaposi sarcoma;
f. Gestational trophoblastic neoplasia;
g. Neuroendocrine and adrenal tumors;
h. Soft tissue sarcoma;
i. Uterine neoplasms;
j. Vaginal cancer;
k. Vulvar cancer;

5. Prescribed as a single agent or in combination with Opdivo for all of the following (a-c);*
   a. Brain metastases;
   b. Merkel cell carcinoma;
   c. Uveal melanoma;

   **Prior authorization may be required for Opdivo.*
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

I. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Melanoma-Unresectable or Metastatic

1. Reauthorization beyond 16 weeks is not permitted. Members must meet the initial approval criteria, at a minimum of 3 months since initial treatment discontinuation.

Approval duration: Not applicable

B. Renal Cell Carcinoma, Colorectal Cancer, Hepatocellular Carcinoma (must meet all):

1. Reauthorization beyond 16 weeks is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

C. Melanoma (Adjuvant Treatment), Non-Small Cell Lung Cancer, Malignant Pleural Mesothelioma, Esophageal Cancer (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;

3. If request is for NSCLC, malignant pleural mesothelioma, or ESCC, maximum duration of therapy does not exceed 2 years;
4. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. For melanoma: New dose does not exceed 3 mg/kg every 12 weeks for up to 4 additional doses;
   b. For NSCLC and malignant pleural mesothelioma, and ESCC: New dose does not exceed 1 mg/kg IV every 6 weeks in combination with Opdivo;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 12 months

D. NCCN Compendium Indications (off-label) (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.PHARM.01) applies; or
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALK: anaplastic lymphoma kinase
BRAF: B-Raf proto-oncogene, serine/ threonine kinase
CPS: combined positive score
CRC: colorectal cancer
CTLA-4: cytotoxic T-lymphocyte antigen 4
dMMR: mismatch repair deficient
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
HCC: hepatocellular carcinoma
MET: mesenchymal-epithelial transition
MSI-H: microsatellite instability-high
PD-1: programmed death-1
PD-L1: programmed death-ligand 1
RCC: renal cell carcinoma
ROS1: ROS proto-oncogene 1

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Nexavar (sorafenib)	**HCC** 400 mg PO BID	800 mg/day
Lenvima (lenvatinib)	**HCC** 12 mg PO QD (patients ≥ 60 kg) or 8 mg PO QD (patients < 60 kg)	12 mg/day
Tecentriq (atezolizumab) + bevacizumab (Avastin®, Mvasi, Zirabev)	**HCC** Tecentriq: 840 mg IV every 2 weeks, 1,200 mg IV every 3 weeks, or 1,680 mg IV every 4 weeks Bevacizumab: 15 mg/kg IV every 3 weeks	See regimen
Imfinzi (durvalumab)*	**HCC** Varies	Varies
platinum-containing regimens	**NSCLC – squamous cell carcinoma** paclitaxel + carboplatin dose varies **NSCLC – nonsquamous cell carcinoma** pemetrexed + [carboplatin or cisplatin] dose varies	Varies
EGFR S768I, L861Q, and/or G719X targeted therapies: afatinib, osimertinib, erlotinib, gefitinib, dacomitinib	**NSCLC** Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications and Boxed Warnings

- Bristol-Myers Squibb was released from the REMS program for Yervoy in March 2015.
- Boxed warning(s): none reported
- Contraindiation(s): none reported

Appendix D: General Information

- NCCN no longer recommends the use of Yervoy for the following indications:
  - Small cell lung cancer
  - NSLCLC with tumor mutation burden, RET rearrangement positive tumors, EGFR exon 19 deletion tumors, exon 21 L858R tumors, ALK rearrangement positive tumors, or ROS1 rearrangement positive tumors
  - Cutaneous melanoma, as adjuvant systemic therapy in combination with Opdivo if no evidence of disease following metastasis-directed therapy or systemic therapy for oligometastatic disease
  - Colon cancer for patients who are not appropriate for intensive therapy

- Hepatocellular carcinoma with tumor mutation burden-high

- Per NCCN, contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK, RET, or ROS1 rearrangements have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Melanoma (adjuvant treatment)	3 mg/kg IV every 3 weeks up to a maximum of 4 doses, followed by 3 mg/kg every 12 weeks for up to 4 additional doses.	3 mg/kg/dose
Melanoma (unresectable or metastatic)	Monotherapy: 3 mg/kg IV every 3 weeks for a maximum of 4 doses In combination with nivolumab: 3 mg/kg every 3 weeks with nivolumab 1 mg/kg for a maximum of 4 doses or until unacceptable toxicity, whichever occurs earlier.	3 mg/kg/dose
RCC	1 mg/kg every 3 weeks with nivolumab 3 mg/kg for a maximum of 4 doses.	1 mg/kg/dose
CRC	1 mg/kg every 3 weeks with nivolumab 3 mg/kg	1 mg/kg/dose
HCC	3 mg/kg every 3 weeks with nivolumab 1 mg/kg for 4 doses	3 mg/kg/dose
NSCLC	In combination with nivolumab: 1 mg/kg every 6 weeks with nivolumab 360 mg every 3 weeks until disease progression, unacceptable toxicity, or up to 2 years in patients without disease progression In combination with nivolumab and platinum-doublet chemotherapy: 1 mg/kg every 6 weeks with nivolumab 360 mg every 3 weeks and 2 cycles of histology-based platinum-doublet chemotherapy every 3 weeks until disease progression, unacceptable toxicity, or up to 2 years in patients without disease progression	1 mg/kg/dose
Malignant pleural mesothelioma	1 mg/kg every 6 weeks with nivolumab 360 mg every 3 weeks until disease progression, unacceptable toxicity, or up to 2 years in patients without disease progression.	1 mg/kg/dose
ESCC	1 mg/kg every 6 weeks with nivolumab 3 mg/kg every 2 weeks or 360 mg every 3 weeks until	1 mg/kg/dose

Indication	Dosing Regimen	Maximum Dose
	disease progression, unacceptable toxicity, or up to 2 years in patients without disease progression.	

V. Product Availability

Single-use vials: 50 mg/10 mL, 200 mg/40 mL

VI. References

1. Yervoy Prescribing information. Princeton, NJ: Bristol-Myers Squibb Company; May 2025. Available at: https://packageinserts.bms.com/pi/pi_yervoy.pdf. Accessed January 30, 2026.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 30, 2026.
3. National Comprehensive Cancer Network. Mesothelioma: Pleural Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/meso_pleural.pdf. Accessed January 30, 2026.
4. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 3.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed January 30, 2026.
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6. National Comprehensive Cancer Network. Hepatocellular Carcinoma, Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf. Accessed January 30, 2026.
7. National Comprehensive Cancer Network. Gastric Cancer, Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed january 30, 2026.
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9. National Comprehensive Cancer Network. Melanoma: Cutaneous, Version 2.2025. Available at: www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed January 30, 2026.
10. National Comprehensive Cancer Network. Kidney Cancer, Version 1.2026. Available at: www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed January 30, 2026.
11. National Comprehensive Cancer Network. Colon Cancer, Version 5.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed January 30, 2026.
12. National Comprehensive Cancer Network. Rectal Cancer, Version 4.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed January 30, 2026.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9228	Injection, ipilimumab, 1 mg

Reviews, Revisions, and Approvals	Date
Criteria added for new FDA indication: advanced renal cell carcinoma in combination with nivolumab; removed malignant pleural mesothelioma due to NCCN 2B recommendation status; added oncologist specialist requirement for all covered indications; summarized NCCN and FDA-approved uses for improved clarity; added up to a total tx duration of 3 years for cutaneous melanoma per PI; added failure of platinum-containing chemotx for SCLC per NCCN; allowed continuity of care for continued approval; clarified continued therapy language for unresectable or metastatic melanoma that reauthorization beyond 16 weeks is not permitted from reauthorization is not permitted; references reviewed and updated.	05/2018
2Q 2019 annual review: criteria added for colorectal cancer in combination with nivolumab; added coverage for malignant pleural mesothelioma; references reviewed and updated.	04/2019
2Q 2020 annual review: criteria added for hepatocellular carcinoma (HCC) in combination with nivolumab; added NCCN compendium-supported indications of small bowel adenocarcinoma, uveal melanoma, non-small cell lung cancer; condensed NCCN compendium-supported indications into one subsection; references reviewed and updated.	04/2020
FDA approved malignant pleural mesothelioma added. Ad hoc changes: melanoma unresectable/metastatic disease and lymph node positive disease criteria sets combined; for HCC, Lenvima added as a prior therapy option per NCCN; for NSCLC, single agent therapy for TMB positive tumor added and combination therapy for RET rearrangement added per NCCN, combination therapy changed from Yervoy and platinum doublet therapy to Yervoy plus/minus a platinum based regimen to accommodate NCCN recommended uses; references reviewed and updated.	01/2021
2Q 2021 annual review: clarified RCC as "advanced or metastatic" per NCCN and prescribing information, removed SCLC from off-label indications as this is no longer supported by NCCN, and removed boxed warning from Appendix C per prescribing information; references reviewed and updated.	04/2021
2Q 2022 annual review: revisions made per NCCN – for melanoma, added pathway for use as a single agent or in combination with Keytruda or Imlygic; for HCC, added additional optional for prior use of Tecentriq + bevacizumab; for NSCLC, removed use in disease positive for tumor mutation burden biomarker, revised requirement for "progression on PD-1/PD-L1 inhibitors" to "no contraindications to PD-1/PD-L1 inhibitors", clarified criteria regarding disease mutation status (unknown status is no longer allowed, and prior targeted therapy is now only required for ROS1 and EGFR S768I, L861Q, and/or G719X mutations), and removed	04/2022

Reviews, Revisions, and Approvals	Date
requirement for PD-L1 ≥ 1% as it is not necessary given allowable compendial uses; for uveal melanoma, added requirement that disease is metastatic; updated Appendix D to reflect NCCN's stance on SCLC and TMB NSCLC; references reviewed and updated.	
2Q 2023 annual review: updated FDA indication for RCC to mirror PI; revised NSCLC criteria to include additional requirements related to mutation status, added off-label use for MSI-H/dMMR ampullary adenocarcinoma, bone cancer, brain metastases, and Kaposi sarcoma per NCCN compendium; criteria added for new FDA approved indication of ESCC in combination with Opdivo; for HCC, added additional option for prior use of Imfinzi and removed requirement for no previous treatment with a checkpoint inhibitor per latest NCCN guidelines; references reviewed and updated.	04/2023
2Q 2024 annual review: for melanoma, added criteria for resectable and limited resectable per NCCN 2A recommendations, removed specification to use combination Opdivo/Yervoy for only unresectable or metastatic melanoma; for colorectal cancer, added indication of POLE/POLD1 mutation per NCCN; for NSCLC ROS1 rearrangement, added reprotrectinib and lorlatinib as prior use option per NCCN; for malignant pleural mesothelioma, revised criteria to allow both unresectable and resectable disease per NCCN; for off-label NCCN compendium indication, added the following indications: MSI-H or dMMR gastric cancer, MSI-H or dMMR esophageal adenocarcinoma, biliary tract cancers, merkel cell carcinoma, and soft tissue sarcoma; references reviewed and updated.	04/2024
2Q 2025 annual review: updated FDA indication for RCC and HCC to mirror PI; for melanoma, clarified combination use with Keytruda is off-label use per NCCN and revised adjuvant treatment maximum dosage per PI; for NSCLC per NCCN, added criteria for NRG1 gene fusion positive; removed criteria for the following mutations: RET rearrangement, EGFR exon 19 deletion, exon 21 L858R, ALK rearrangement, ROS1 rearrangement; for ESCC per NCCN, added off-label indication for prescribed as induction systemic therapy; for off-label NCCN compendium indications, consolidated MSI-H/dMMR cancers, revised biliary tract cancer criteria to allow primary treatment; in Appendix B, removed entries that are not redirections (Opdivo and Keytruda); in Appendix D, added no longer recommended indications; in Section V, clarified dosing regimen wording per PI; references reviewed and updated. RT4: updated FDA Approved Indication(s) section and criteria to reflect revised indication that limits use to tumors expressing PD-L1 (≥ 1) for unresectable advanced or metastatic ESCC in combination with Yervoy per updated PI (previously approved regardless of PD-L1 status); also for ESCC, added option to be prescribed as palliative therapy and clarified when prescribed as induction, neoadjuvant, perioperative, or palliative therapy that tumor is characterized as MSI-H or dMMR.	04/2025

Reviews, Revisions, and Approvals	Date
2Q 2026 annual review: for melanoma, NSCLC, malignant pleural mesothelioma, ESCC, and off-label NCCN compendium indications, extended initial approval durations from 6 months to 12 months for this maintenance medication for a chronic condition; for NSCLC, malignant pleural mesothelioma, and ESSC continued therapy, added criterion for maximum duration of therapy limit of 2 years; for ESCC, added option to be prescribed as induction therapy; for off-label NCCN compendium indications, removed use as a single agent for soft tissue sarcoma, added off-label indications for appendiceal neoplasms and cancers, small bowel adenocarcinoma with POLE/POLD mutation, cervical cancer, neuroendocrine and adrenal tumors, uterine neoplasms, vaginal cancer, and vulvar cancer; references reviewed and updated.	04/2026