

## Clinical Policy: Ipilimumab (Yervoy)

Reference Number: PA.CP.PHAR.319

Effective Date: 01/2018

Last Review Date: 04/2024

### Description

Ipilimumab (Yervoy<sup>®</sup>) is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody.

### FDA Approved Indication(s)

Yervoy is indicated for:

- **Unresectable or metastatic 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
- **Adjuvant treatment of melanoma**
  - 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 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) metastatic CRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, in combination with nivolumab\*
- **Hepatocellular carcinoma (HCC)**
  - In combination with nivolumab, the treatment of patients with 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)  $\geq 1\%$  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

\*This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

### 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<sup>®</sup> 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, or c):
  - a. Unresectable or metastatic;
  - b. Resectable, limited resectable, or lymph node positive;
  - c. Recurrent
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:  $\geq 12$  years;
  - b. For adjuvant treatment:  $\geq 18$  years;
4. Prescribed in one of the following ways (a, b, c or d):
  - a. As a single agent;
  - b. In combination with Opdivo<sup>®\*</sup>;
  - c. In combination with Keytruda<sup>®\*</sup> for unresectable or metastatic melanoma;
  - d. In combination with Imlygic<sup>®\*</sup> 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 10 mg/kg every 3 weeks for 4 doses, followed by 10 mg/kg every 12 weeks for up to 3 years;
  - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 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  $\geq 12$  years;
4. Prescribed in combination with Opdivo<sup>®</sup>;  
*\*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  $\geq$  12 years;
4. Disease is advanced, progressive, unresectable or metastatic;
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  $\geq$  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  $\geq$  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-f):\*
  - a. Disease mutation status is negative for actionable biomarkers (EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET and ERBB2 [HER2]), and member has not received prior systemic therapy for advanced disease;
  - 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 19 deletion or L858R, and member has received prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib;\*
  - d. Disease mutation status is positive for ROS1 rearrangement, and member has received prior crizotinib, entrectinib, repotrectinib, lorlatinib, or ceritinib;
  - e. Disease mutation status is positive for ALK rearrangement, and member has received prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib;\*
  - f. Disease mutation status is positive for EGFR exon 20, KRAS G12C, NRTK1/2/3, BRAF V600E, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2);  
*\*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: 6 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: 6 months**

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

- 1. Diagnosis of unresectable advanced, recurrent, or metastatic ESCC;
- 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: 6 months**

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

- 1. Diagnosis of one of the following (a-1):
  - a. MSI-H, dMMR, or POLE/POLD1 mutation small bowel adenocarcinoma;
  - b. Metastatic or unresectable uveal melanoma;
  - c. MSI-H or dMMR ampullary adenocarcinoma;
  - d. MSI-H or dMMR gastric cancer;

- e. MSI-H or dMMR esophageal adenocarcinoma;
- f. 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;
- g. BRAF non-specific melanoma brain metastases;
- h. Classic Kaposi sarcoma as subsequent systemic therapy;
- i. Biliary tract cancer (e.g., gallbladder, intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma), as subsequent therapy;
- j. Merkel cell carcinoma;
- k. Soft tissue sarcoma and one of the following (i or ii):
  - i. Disease is angiosarcoma;
  - ii. Prescribed as subsequent therapy for advanced or metastatic disease, and disease is one of the following (1-6):
    - 1. Tumor mutation burden-high ( $\geq 10$  mutations per megabase);
    - 2. Myxofibrosarcoma;
    - 3. Undifferentiated pleomorphic sarcoma;
    - 4. Dedifferentiated liposarcoma;
    - 5. Cutaneous angiosarcoma;
    - 6. Undifferentiated sarcomas;
- 1. Other NCCN recommendations listed as category 1, 2A, or 2B;
- 2. Prescribed by or in consultation with an oncologist;
- 3. Age  $\geq 12$  years;
- 4. Prescribed in combination with Opdivo for all of the following (a-g):\*
  - a. MSI-H/dMMR/POLE/POLD1 mutation small bowel adenocarcinoma;
  - b. MSI-H/dMMR ampullary adenocarcinoma;
  - c. MSI-H or dMMR gastric cancer;
  - d. MSI-H or dMMR esophageal adenocarcinoma;
  - e. Bone cancer;
  - f. Classic Kaposi sarcoma;
  - g. Biliary tract cancer;
- 5. Prescribed as a single agent or in combination with Opdivo for all of the following (a-d):\*
  - a. Uveal melanoma;
  - b. Brain metastases;
  - c. Merkel cell carcinoma;
  - d. Soft tissue sarcoma;

*\*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: 6 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.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. 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 10 mg/kg every 12 weeks for up to 3 years;
  - 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 or up to a total duration of 3 years (cutaneous melanoma) or 2 years (NSCLC, malignant pleural mesothelioma, ESCC), whichever is less**

### 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.LTSS.PHAR.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.LTSS.PHAR.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

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
Opdivo® (nivolumab)	<p><b>MSI-H/dMMR small bowel adenocarcinoma</b> 3 mg/kg IV once every 3 weeks for four doses, then 3 mg/kg IV or 240 mg IV every 2 weeks with or without ipilimumab</p> <p><b>Unresectable or metastatic melanoma</b> <u>Adult and pediatric weighing ≥ 40 kg:</u> nivolumab 1 mg/kg every 3 weeks for four doses in combination with ipilimumab 3 mg/kg every 3 weeks, then nivolumab 240 mg every 2 weeks or 480 mg every 4 weeks as a single agent until disease progression or unacceptable toxicity</p> <p><u>Pediatric weighing &lt; 40 kg:</u> nivolumab 1 mg/kg every 3 weeks for four doses in combination with ipilimumab 3 mg/kg every 3 weeks, then nivolumab 3 mg/kg every 3 weeks or 6 mg/kg mg every 6 weeks as a single agent until disease progression or unacceptable toxicity</p>	<p>RCC, HCC, melanoma: 480 mg/dose</p> <p>CRC, small bowel adenocarcinoma, pediatric (weighing &lt; 40 kg) melanoma: 240 mg/dose</p>
Keytruda (pembrolizumab)	<p><b>Melanoma</b> Adult: 200 mg every 3 weeks or 400 mg every 6 weeks Pediatric: 2 mg/kg (up to 200 mg) every 3 weeks</p>	See regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Nexavar (sorafenib)	<b>HCC</b> 400 mg PO BID	800 mg/day
Lenvima (lenvatinib)	<b>HCC</b> 12 mg PO QD (patients $\geq$ 60 kg) or 8 mg PO QD (patients < 60 kg)	12 mg/day
Tecentriq (atezolizumab) + bevacizumab (Avastin <sup>®</sup> , Mvasi, Zirabev)	<b>HCC</b> 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)*	<b>HCC</b> Varies	Varies
platinum-containing regimens	<b>NSCLC – squamous cell carcinoma</b> paclitaxel + carboplatin dose varies  <b>NSCLC – nonsquamous cell carcinoma</b> pemetrexed + [carboplatin or cisplatin] dose varies	Varies
EGFR S768I, L861Q, and/or G719X targeted therapies: afatinib, osimertinib, erlotinib, gefitinib, dacomitinib	<b>NSCLC</b> Varies	Varies
ROS1 targeted therapies: crizotinib, entrectinib, ceritinib	<b>NSCLC</b> Varies	Varies

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) 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
- Contraindication(s): none reported

#### Appendix D: General Information

- NCCN no longer recommends the use of Yervoy for the following indications:
  - Small cell lung cancer
  - Tumor mutation burden NSCLC
  - 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
- 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, or presence of an oncogene (i.e., EGFR exon 19 deletion or L858R, ALK rearrangements), which would predict lack of benefit.

**IV. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Melanoma (adjuvant treatment)	10 mg/kg IV every 3 weeks for 4 doses, followed by 10 mg/kg every 12 weeks for up to 3 years or until documented disease recurrence or unacceptable toxicity.	10 mg/kg/dose
Melanoma (unresectable or metastatic)	<p><u>Monotherapy:</u> 3 mg/kg IV every 3 weeks for a total of 4 doses</p> <p><u>In combination with nivolumab:</u> 3 mg/kg every 3 weeks with nivolumab 1 mg/kg for a maximum of 4 doses or until unacceptable toxicity, whichever occurs earlier.</p>	3 mg/kg/dose
RCC	Nivolumab 3 mg/kg IV, followed by ipilimumab 1 mg/kg IV on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks	1 mg/kg/dose
CRC	Nivolumab 3 mg/kg IV, followed by ipilimumab 1 mg/kg IV on the same day, every 3 weeks for a maximum of 4 doses or until intolerable toxicity or disease progression, then nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks	1 mg/kg/dose
HCC	Nivolumab 1 mg/kg IV, followed by ipilimumab 3 mg/kg IV on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks	3 mg/kg/dose
NSCLC	<p><u>In combination with nivolumab:</u> nivolumab 3 mg/kg IV every 2 weeks and ipilimumab 1 mg/kg IV every 6 weeks until disease progression, unacceptable toxicity, or for up to 2 years in patients without disease progression</p> <p><u>In combination with nivolumab and platinum-doublet chemotherapy:</u> nivolumab 360 mg IV every 3 weeks and ipilimumab 1 mg/kg IV every 6 weeks and histology-based platinum-doublet chemotherapy every 3 weeks for 2 cycles until disease</p>	1 mg/kg/dose

Indication	Dosing Regimen	Maximum Dose
	progression, unacceptable toxicity, or up to 2 years in patients without disease progression	
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 disease progression, unacceptable toxicity, or up to 2 years in patients without disease progression.	1 mg/kg/dose

**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; February 2023. Available at: [https://packageinserts.bms.com/pi/pi\\_yervoy.pdf](https://packageinserts.bms.com/pi/pi_yervoy.pdf). Accessed February 7, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed February 22, 2024.
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5. Hellman MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. *N Engl J Med*. 2019 November; 381(21):2020-2031.
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9. National Comprehensive Cancer Network. Kidney Cancer, Version 2.2024. Available at: [www.nccn.org/professionals/physician\\_gls/pdf/kidney.pdf](http://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf). Accessed February 7, 2024.
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11. National Comprehensive Cancer Network. Rectal Cancer, Version 1.2024. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/rectal.pdf](https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf). Accessed February 7, 2024.

**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 Tecentrig +	04/2022

Reviews, Revisions, and Approvals	Date
<p>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 requirement for PD-L1 <math>\geq 1\%</math> 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.</p>	
<p>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.</p>	04/2023
<p>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.</p>	04/2024