Ipilimumab (Yervoy®)	Place of Service Office Administration Outpatient Facility Infusion Administration Infusion Center Administration HCPCS: **J9228** per 1 mg

Condition(s) listed in policy (*see criteria for details*)

- Ampullary adenocarcinoma
- Appendiceal cancer
- Colorectal cancer
- Esophageal and esophagogastric junction squamous cell carcinoma
- Hepatocellular carcinoma
- Melanoma: cutaneous
- Melanoma: uveal
- Mesothelioma: peritoneal
- Mesothelioma: pleural
- Non-small cell lung cancer
- Renal cell carcinoma
- Small bowel adenocarcinoma
- Soft tissue sarcoma

AHFS therapeutic class: Antineoplastic agent

Mechanism of action: Ipilimumab is a recombinant, human monoclonal antibody that binds to the cytotoxic T- lymphocyte-associated antigen 4 (CTLA-4). The mechanism of action of ipilimumab's effect in patients with melanoma is indirect, possibly through T-cell mediated antitumor immune responses

(1) Special Instructions and Pertinent Information

Covered under the Medical Benefit, please submit clinical information for prior authorization review via fax.

(2) Prior Authorization/Medical Review is required for the following condition(s)

All requests for Yervoy® (ipilimumab) must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Ampullary adenocarcinoma

1. Attestation of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), **AND**
2. Used in combination with Opdivo for 4 doses, followed by Opdivo as a single agent, **AND**
3. Either of the following:
    a. First line therapy for intestinal type disease, or
    b. Subsequent therapy

Covered Doses
Combination therapy:
Yervoy 3 mg/kg IV with Opdivo 1 mg/kg IV every 3 weeks for 4 doses, followed by Opdivo as a single agent

Coverage Period
Indefinitely

ICD-10:
C24.1

Appendiceal or Colorectal cancer

1. Attestation of microsatellite instability-high (MSI-H) and/or defective mismatch repair (dMMR), **AND**
2. Used in combination with Opdivo, **AND**
3. Meets either of the following:
    a. Used for neoadjuvant treatment of resectable advanced (e.g., T4b) or resectable metastatic disease, OR
    b. Used for unresectable advanced or metastatic disease

Covered Doses
Yervoy 1 mg/kg IV every 3 weeks with Opdivo 3 mg/kg IV every 3 weeks for 4 doses, followed by Opdivo as a single agent thereafter

Coverage Period
Cover 4 doses in 16 weeks

ICD-10:
C17.0-C17.2, C17.8, C17.9, C18.0-C18.9, C19, C20, C21.8

Esophageal and esophagogastric junction squamous cell carcinoma

1. One of the following:
    a. Disease is unresectable locally advanced, recurrent, or metastatic, or
    b. Patient is not a surgical candidate

AND

2. First-line therapy, **AND**
3. Combination with Opdivo

Covered Doses
Yervoy 1 mg/kg IV every 6 weeks with Opdivo 3 mg/kg IV every 2 weeks

Coverage Period
2 years

ICD-10:
C15.3-C15.5, C15.8, C15.9, C16.0, D37.8, D37.9, Z85.00, Z85.01

Hepatocellular carcinoma

1. Disease has progressed on or after prior systemic therapy, **AND**
2. Being used in combination with Opdivo

Covered Doses

Yervoy 3 mg/kg IV every 3 weeks with Opdivo (1mg/kg) for 4 doses, followed by Opdivo as a single agent thereafter

Coverage Period
Cover for 4 doses total

ICD-10:
C22.0, C22.9

Melanoma: cutaneous

1. Either of the following:
    a. Adjuvant treatment AND meets all of the following:
        i. Single agent therapy and prior exposure to an anti-PD1 therapy, or
        ii. Combination therapy with Opdivo

    OR

    b. Unresectable or metastatic disease, AND meets one of the following:
        i. Single agent therapy, OR
        ii. Combination therapy with Opdivo, OR
        iii. Combination therapy with Keytruda and has had disease progression on an anti-PD-1 immunotherapy drug

Covered Doses and Coverage Period
Adjuvant
Single agent:
10 mg/kg IV every 3 weeks for 4 doses, followed by 10 mg/kg every 12 weeks for up to 3 years
Combination:
With Opdivo:
Yervoy 3 mg/kg IV every 3 weeks with Opdivo 1 mg/kg IV for a total of 4 doses, followed by Opdivo as a single agent for 1 year

Unresectable or metastatic
Single agent:
10 mg/kg IV every 3 weeks for 4 doses, followed by 10 mg/kg every 12 weeks thereafter indefinitely, OR
Combination:
With Opdivo:
Yervoy 1 mg/kg IV every 3 weeks with Opdivo 3 mg/kg every 3 weeks for a total of 4 doses, followed by Opdivo as a single agent thereafter
OR
Yervoy 3 mg/kg IV every 3 weeks with Opdivo 1 mg/kg IV for a total of 4 doses, followed by Opdivo as a single agent thereafter
With Keytruda:
Yervoy 1 mg/kg IV every 3 weeks with Keytruda 200 mg every 3 weeks, for a total of 4 doses, followed by Keytruda as a single agent thereafter

Re-induction of 4 doses (as a single agent or in combination with anti-PD-1 therapy) may be covered if prior use resulted in a clinical response or stable disease and disease progressed or relapsed greater than 3 months following treatment discontinuation

ICD-10:
C43.0, C43.10-C43.12, C43.20-C43.22, C43.30, C43.31, C43.39, C43.4, C43.51, C43.52, C43.59-C43.62, C43.70-C43.72, C43.8, C43.9

Melanoma: uveal

1. Being used for metastatic disease as a single agent, or in combination with Opdivo for the first 4 doses followed by Opdivo as a single agent

Covered Doses and Coverage Period
Single agent:
Yervoy 3 mg/kg IV every 3 weeks for 4 doses

Combination therapy:
Yervoy 3 mg/kg IV every 3 weeks with Opdivo 1 mg/kg IV for 4 doses, followed by Opdivo as a single agent thereafter

ICD-10:
C69.30-C69.32, C69.40 -C69.42, C69.60-C69.62

Mesothelioma: peritoneal

1. Either of the following:
   a. First line therapy for unresectable disease in combination with Opdivo, OR
   b. Subsequent use in combination with Opdivo (if not used first-line)

Covered Doses
Combination therapy:
Yervoy 1 mg/kg IV every 6 weeks, with Opdivo 3 mg/kg IV every 2 weeks/ 360 mg IV every 3 weeks

Coverage Period
Indefinitely

ICD-10:
C45.1

Mesothelioma: pleural

1. Being used in combination with Opdivo

Covered Doses
Combination therapy:
Yervoy 1 mg/kg IV every 6 weeks, with Opdivo 3 mg/kg IV every 2 weeks / 360 mg IV every 3 weeks

Coverage Period
Indefinite

ICD-10:
C38.4, C45.0

Non-small cell lung cancer

1. Disease is recurrent, advanced or metastatic, **AND**
2. One of the following:
   a. Used in combination with Opdivo, or
   b. Used in combination with Opdivo, paclitaxel, and carboplatin, or

c. Used in combination with Opdivo, Alimta, and a platinum drug (carboplatin or cisplatin)

Covered Doses and Coverage Period

Single agent:
Yervoy 1 mg/kg IV every 6 weeks indefinitely
Combination:
With Opdivo:
Yervoy 1 mg/kg IV every 6 weeks, with Opdivo 3 mg/kg IV every 2 weeks indefinitely
OR
Yervoy 3 mg/kg IV every 3 weeks with Opdivo 1 mg/kg IV every 3 weeks for doses, followed by Opdivo as a single agent thereafter

With Opdivo, Alimta/Paclitaxel, and Carboplatin/Cisplatin:
Cycle One (42-day cycle):

- Yervoy 1 mg/kg IV on Day 1
- Opdivo 360 mg IV on Days 1 and 22
- Pemetrexed 500 mg/m^2 IV on Days 1 and 22, or Paclitaxel 200 mg/m^2 IV on Days 1 and 22
- Carboplatin AUC 6 IV on Days 1 and 22, or Cisplatin 75 mg/m^2 IV on Days 1

Followed by:
Cycle two and after (42-day cycles): Yervoy 1 mg/kg IV on Day 1, with Opdivo 360 mg IV on Days 1 and 22, indefinitely

ICD-10:
C33, C34.00-C34.02, C34.10-C34.12, C34.2, C34.30-C34.32, C34.80-C34.82, C34.90-C34.92, Z85.118

Renal cell carcinoma

1. Advanced disease, **AND**
2. Being used in combination with Opdivo for 4 cycles, followed by Opdivo as a single agent

Covered Doses
Yervoy 1 mg/kg IV every 3 weeks with Opdivo 3 mg/kg IV for 4 doses, followed by Opdivo single agent thereafter

Coverage Period
Cover 4 doses in 16 weeks

ICD-10:
C64.1, C64.2, C64.9, C65.1, C65.2, C65.9, Z85.528

Small bowel adenocarcinoma

1. Advanced or metastatic disease, **AND**
2. Attestation of high microsatellite instability (MSI-H) and/or defective mismatch repair (dMMR), **AND**
3. No prior treatment with a PD-1 PD-L1 immune checkpoint inhibitor therapy, **AND**
4. Used in combination with Opdivo, **AND**
5. Either of the following:
    a. First-line therapy, OR
    b. Subsequent therapy, and no prior oxaliplatin exposure in the adjuvant setting or contraindication to oxaliplatin

Covered Doses
Combination therapy:
Yervoy 1 mg/kg IV every 3 weeks, with Opdivo 3 mg/kg IV every 3 weeks, for 4 doses followed by

Opdivo as a single agent of 3 mg/kg IV every 2 weeks/ 240 mg every 2 weeks thereafter

Coverage Period
Cover 4 doses in 16 weeks

ICD-10:
C17.0, C17.1, C17.2, C17.3, C17.8, C17.9, Z85.068

Soft tissue sarcoma

1. Either of the following:
    a. Used for non-cutaneous angiosarcoma in combination with Opdivo, **OR**
    b. Used for advanced/metastatic or unresectable disease, **AND**
        i. Used in combination with Opdivo, **and**
        ii. Used as subsequent therapy, **and**
        iii. Meets one of the following:
            1. Myxofibrosarcoma, undifferentiated pleomorphic sarcoma, pleomorphic rhabdomyosarcoma, dedifferentiated liposarcoma, cutaneous angiosarcoma, or undifferentiated sarcomas

            Or

            2. Tumor mutational burden-high (TMB-H) [10 mutations/ megabase (mut/Mb)] STS

Covered Doses
Yervoy 1 mg/kg IV every 6 weeks

Coverage Period
Indefinite

ICD-10:
C22.3, C47.0, C47.10-C47.12, C47.20-C47.22, C47.3, C47.4- C47.6, C47.8, C47.9, C48.0-C48.2, C48.8, C49.0, C49.10-C49.12, C49.20-C49.22, C49.3-C49.6, C49.8, C49.9, Z85.831

(3) The following condition(s) DO NOT require Prior Authorization/Preservice
All requests for Yervoy® (ipilimumab) must be sent for clinical review and receive authorization prior to drug administration or claim payment.

(4) This Medication is NOT medically necessary for the following condition(s)
Coverage for a Non-FDA approved indication, requires that criteria outlined in Health and Safety Code § 1367.21, including objective evidence of efficacy and safety are met for the proposed indication.

Please refer to the Provider Manual and User Guide for more information.

(5) Additional Information
How Supplied:
50 mg, 200 mg (single-use vials)

(6) References

- AHFS®. Available by subscription at http://www.lexi.com

- DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
- National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium. Yervoy® (2023). Available by subscription at: www.nccn.org.
- National Comprehensive Cancer Network. Ampullary Adenocarcinoma (Version 2.2022). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Biliary Tract Cancers (Version 1.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Central Nervous System Cancers (Version 1.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Colon Cancer. (Version 1.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Esophageal and esophagogastric junction cancers (Version 2.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Hepatocellular carcinoma (Version 1.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Melanoma: Cutaneous (Version 2.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Melanoma: Uveal (Version 2.2022). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Kidney Cancer (Version 4.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Mesothelioma: Peritoneal (Version 1.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Mesothelioma: Pleural (Version 1.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Non-Small Cell Lung Cancer (Version 2.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Rectal cancer (Version 1.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Small Bowel Adenocarcinoma (Version 1.2023). Available at: www.nccn.org/
- National Comprehensive Cancer Network. Soft Tissue Sarcoma. (Version 2.2023). Available at: www.nccn.org/
- Yervoy® (ipilimumab) [Prescribing Information]. Princeton, NJ: Bristol-Myers Squibb. 2/2023.

(7) Policy Update

Date of of last revision: 3Q2023
Date of next review: 2Q2024
Changes from previous policy version:

- New indication in Section (2): Added coverage for soft tissue sarcoma
  Rationale: NCCN category 2A support

BSC Drug Coverage Criteria to Determine Medical Necessity
Reviewed by P&T Committee