Yervoy® (ipilimumab)
(Intravenous)

Document Number: IC-0148

Last Review Date: 09/01/2021
Date of Origin: 11/28/2011
Dates Reviewed: 12/2011, 03/2012, 06/2012, 09/2012, 12/2012, 05/2013, 06/2013, 09/2013, 12/2013, 03/2014, 06/2014, 09/2014, 12/2014, 03/2015, 05/2015, 08/2015, 10/2015, 11/2015, 02/2016, 05/2016, 08/2016, 11/2016, 01/2017, 05/2017, 08/2017, 11/2017, 02/2018, 05/2018, 08/2018, 12/2018, 03/2019, 06/2019, 09/2019, 12/2019, 03/2020, 04/2020, 6/2020, 09/2020, 11/2020, 03/2021, 06/2021, 09/2021

I. Length of Authorization [1,6,8-12,17-19,20,24,27-29,33,39-42]

Coverage will be provided for six months and may be renewed (unless otherwise specified).

- The following indications may be renewed up to a maximum of twelve (12) weeks of therapy and may not be renewed *(coverage may be extended to 16 weeks if 4 doses were not administered within the 12 week time frame)*:
  - Colorectal Cancer *(disease progression or after primary treatment)*
  - CNS metastases from Melanoma *(combination therapy with nivolumab)*
  - Cutaneous Melanoma *(first-line or subsequent therapy)*
    ***** *Requests for Cutaneous Melanoma may be renewed if the patient meets the provisions for re-induction therapy.*
  - Hepatocellular Carcinoma (HCC)
  - Renal Cell Carcinoma (RCC)
  - Small Bowel Adenocarcinoma (SBA)/Advanced Ampullary Cancer
  - Uveal Melanoma

Non-Small Cell Lung Cancer (NSCLC)/ Malignant Pleural Mesothelioma

- Coverage will be provided for up to a maximum of 2 years of therapy.

Cutaneous Melanoma (adjuvant therapy)

- Coverage for adjuvant treatment will be provided for six months and may be renewed for up to a maximum of 3 years of therapy.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Yervoy 200 mg/40 mL injection:
  - 5 vials per 84 days (initially up to 5 vials per 21 days x 4 doses)
- Yervoy 50 mg/10 mL injection:
  - 3 vials per 84 days (initially up to 3 vials per 21 days x 4 doses)

Proprietary & Confidential
© 2021 Magellan Health, Inc.

B. Max Units (per dose and over time) [HCPCS Unit]:

Indication	Billable Units (BU)	Per unit time (days)
HCC	350 BU	21 days x 4 doses
Cutaneous Melanoma, CNS metastases	Initial: 1150 BU	Initial: 21 days x 4 doses
	Followed by: 1150 BU	Followed by: 84 days
Uveal Melanoma	1150 BU	21 days x 4 doses
RCC, SBA/Advanced Ampullary Cancer	115 BU	21 days x 4 doses
CRC, MPM, NSCLC	115 BU	42 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age, unless otherwise indicated; **AND**

Cutaneous Melanoma † ‡ Φ [1,2,6,17]

- Used as first-line therapy for unresectable or metastatic disease in combination with nivolumab †; **OR**
- Used as subsequent therapy for unresectable or metastatic* disease; **AND**
    - Used after disease progression or maximum clinical benefit from BRAF-targeted therapy (e.g., dabrafenib/trametinib, vemurafenib/cobimetinib, encorafenib/binimetinib, etc.); **AND**
        - Used as a single agent in patients at least 12 years of age if not previously used alone or in combination with anti-PD-1 immunotherapy †; **OR**
        - Used in combination with nivolumab if not previously used or for patients who progress on single agent anti-PD-1 immunotherapy; **OR**
        - Used in combination with pembrolizumab if not previously used or for patients who progress on single agent anti-PD-1 immunotherapy; **OR**
    - Used for retreatment of disease as re-induction as a single agent or in combination with anti-PD-1 immunotherapy in patients who experienced disease control *(i.e., complete or partial response or stable disease)* from prior checkpoint inhibitor therapy, but subsequently have disease progression/relapse > 3 months after treatment discontinuation; **AND**
        - Patient has completed initial induction ipilimumab therapy (i.e., completion of 4 cycles within a 16 week period); **OR**
- Used as a single-agent for adjuvant therapy; **AND**
    - Patient has pathologic involvement of regional lymph nodes of more than 1 mm and has undergone complete resection including total lymphadenectomy †; **OR**
    - Patient has previously received anti-PD-1 therapy (e.g., nivolumab or pembrolizumab); **AND**
        - Patient has local satellite/in-transit recurrence and has no evidence of disease (NED) after complete excision ‡; **OR**
        - Patient has undergone therapeutic lymph node dissection (TLND) and/or complete resection of nodal recurrence ‡; **OR**

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

- Patient has undergone complete resection of distant metastatic disease ‡

**Metastatic disease includes stage III clinical satellite/in transit metastases or local satellite/in-transit recurrence in patients with limited resectable and unresectable disease, unresectable nodal recurrence, and disseminated (unresectable) distant metastatic disease.*

Uveal Melanoma ‡ [2,20-23,32]

- Used as a single agent or in combination with nivolumab; **AND**
- Patient has distant metastatic disease

Renal Cell Carcinoma (RCC) † ‡ [1,2,18]

- Used in combination with nivolumab for clear cell histology; **AND**
  - Used as first-line therapy in patients with advanced, relapsed, or stage IV disease with poor or intermediate risk; **OR**
  - Used as first-line therapy in patients with relapsed or stage IV disease with favorable risk; **OR**
  - Used as subsequent therapy in patients with relapsed or stage IV disease

Non-Small Cell Lung Cancer (NSCLC) † ‡ [1,2,16,24]

- Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
  - Used as first-line therapy; **AND**
    - Used for one of the following:
      - Patients with PS 0-1 who have tumors that are negative for actionable molecular markers** and PD-L1 <1%
      - Used in patients with PS 0-1 who are positive for one of the following molecular markers: BRAF V600E-mutation, NTRK 1/2/3 gene fusion, or MET exon 14 skipping mutation
      - PD-L1 expression positive (PD-L1 ≥1%) tumors, as detected by an FDA or CLIA compliant test❖, that are negative for actionable molecular markers**; **AND**
        - Used in combination with nivolumab; **OR**
        - Used in combination with nivolumab and platinum-doublet chemotherapy (e.g., pemetrexed and either carboplatin or cisplatin for non-squamous cell histology, or paclitaxel and carboplatin for squamous cell histology, etc.); **OR**
  - Used as subsequent therapy; **AND**
    - Used for one of the following:
      - Patients with PS 0-1 who have ROS1 positive tumors and have received prior targeted therapy§

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

- Patients with PS 0-1 who are positive for one of the following molecular markers: BRAF V600E mutation, NTRK 1/2/3 gene fusion, or MET exon 14 skipping mutation; **AND**
  - Used in combination with nivolumab; **OR**
  - Used in combination with nivolumab, pemetrexed, and either carboplatin or cisplatin for nonsquamous cell histology; **OR**
  - Used in combination with nivolumab, paclitaxel and carboplatin for squamous cell histology; **OR**
- Used as continuation maintenance therapy in combination with nivolumab; **AND**
  - Patient has achieved a response or stable disease following first-line therapy with nivolumab and ipilimumab with or without chemotherapy

*** Note: Actionable molecular genomic biomarkers include EGFR, ALK, ROS1, BRAF, NTRK1/2/3, MET exon 14 skipping mutation, and RET rearrangement. If there is insufficient tissue to allow testing for all of EGFR, ALK, ROS1, BRAF, NTRK1/2/3, MET, and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*

Malignant Pleural Mesothelioma † ‡ Φ [1,2,5,25,26,34,37]

- Used in combination with nivolumab; **AND**
  - Used as subsequent therapy; **OR**
  - Used as first-line therapy in patients with stage IIIB or IV disease, sarcomatoid histology, medically inoperable tumors, or unresectable disease

Central Nervous System (CNS) Cancer ‡ [2,4,8,10,11,27]

- Used for the treatment of brain metastases in patients with melanoma; **AND**
- Used in combination with nivolumab or as a single agent; **AND**
  - Used as initial treatment in patients with small asymptomatic brain metastases; **OR**
  - Used for relapsed disease in patients with limited brain metastases and either stable systemic disease or reasonable systemic treatment options; **OR**
  - Patient has recurrent limited brain metastases; **OR**
  - Used for recurrent disease in patients with extensive brain metastases and stable systemic disease or reasonable systemic treatment options

Colorectal Cancer † ‡ [1,2,19,31,42]

- Patient is at least 12 years of age; **AND**
- Patient's disease must be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); **AND**
- Used in combination with nivolumab*****; **AND**
  - Used for advanced or metastatic disease that progressed following treatment with one of the following:

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

- Fluoropyrimidine-, oxaliplatin-, and/or irinotecan-based chemotherapy † ‡; **OR**
- Non-intensive therapy ‡; **OR**

  - Used as primary treatment for unresectable or medically inoperable, locally advanced, or metastatic disease *(excluding use as neoadjuvant therapy in rectal cancer)* ‡; **OR**
  - Used for unresectable (or medically inoperable) metastases that remain unresectable after primary systemic therapy ‡

** Single agent nivolumab should be used in patients who are not candidates for intensive therapy*

Small Bowel Adenocarcinoma/Advanced Ampullary Cancer ‡ [2,19,29]

- Patient has advanced or metastatic disease that is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); **AND**
- Patient has not previously received treatment with a checkpoint inhibitor (e.g., nivolumab, pembrolizumab, etc.); **AND**
- Used in combination with nivolumab; **AND**
  - Used as initial therapy; **OR**
  - Used as subsequent therapy for patients with no prior oxaliplatin exposure in the adjuvant treatment setting and no contraindication to oxaliplatin therapy

Hepatocellular Carcinoma (HCC) † ‡ [1,2,30]

- Used in combination with nivolumab; **AND**
- Patient has unresectable or metastatic disease, inoperable *(i.e., by performance status, comorbidity or with minimal or uncertain extrahepatic-disease)* liver-confined disease, or disease with extensive liver tumor burden; **AND**
- Used as subsequent therapy; **AND**
- Patient has Child-Pugh Class A disease

❖ *If confirmed using an immunotherapy assay-http://www.fda.gov/CompanionDiagnostics*

† FDA approved indication(s); ‡ Compendia recommended indication; **Φ** Orphan Drug

Genomic Aberration/Mutational Driver Targeted Therapies (Note: *not all inclusive, refer to guidelines for appropriate use*) §				
Sensitizing *EGFR* mutation-positive tumors	*ALK* rearrangement-positive tumors	*ROS1* rearrangement-positive tumors	*BRAF* V600E-mutation positive tumors	*NTRK* Gene Fusion positive tumors
– Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab *(exon-20 insertion)*	– Alectinib – Brigatinib – Ceritinib – Crizotinib – Lorlatinib	– Ceritinib – Crizotinib – Entrectinib	– Dabrafenib ± Trametinib – Vemurafenib	– Larotrectinib – Entrectinib
PD-1/PD-L1 expression-positive tumors (≥1%)	*MET* Exon-14 skipping mutations	*RET* rearrangement-positive tumors	KRAS G12C mutations	
– Pembrolizumab	– Capmatinib	– Selpercatinib	– Sotorasib	

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

– Atezolizumab – Nivolumab ± ipilimumab	– Crizotinib – Tepotinib	– Cabozantinib – Vandetanib – Pralsetinib		

IV. Renewal Criteria [1,2,6,9-12,17-29,39-41]

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: immune-mediated reactions (e.g., colitis, hepatitis, dermatitis/skin adverse reactions, pneumonitis, nephritis/renal dysfunction, endocrinopathies, etc.), severe infusion reactions, etc.; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Coverage may not be renewed for the following indications:
  - Renal Cell Carcinoma (RCC)
  - Colorectal Cancer *(disease progression or after primary treatment)*
  - Small Bowel Adenocarcinoma (SBA)/Advanced Ampullary Cancer
  - Hepatocellular Carcinoma (HCC)
  - Cutaneous Melanoma *(first-line or subsequent therapy)*
  - Uveal Melanoma
  - CNS metastases from melanoma *(combination therapy with nivolumab)*

Cutaneous Melanoma (re-induction therapy)

- *Refer to Section III for criteria (see Cutaneous Melanoma – Used for retreatment of disease as re-induction)*

Cutaneous Melanoma Maintenance therapy (adjuvant treatment)

- Patient has not exceeded a maximum of three (3) years of therapy

Non-Small Cell Lung Cancer (in combination with nivolumab with or without platinum-doublet chemotherapy)

- Patient has not exceeded a maximum of two (2) years of therapy

Non-Small Cell Lung Cancer (maintenance therapy)

- *Refer to Section III for criteria*

MPM

- Patient has not exceeded a maximum of two (2) years of therapy

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

V. Dosage/Administration [1,6,8-12,17-29,33,34,39-42]

Indication	Dose
Cutaneous Melanoma *(excluding adjuvant therapy)*	Single agent or in combination with nivolumab: o Administer 3 mg/kg intravenously every 3 weeks for a maximum of 4 doses (when given in combination with nivolumab, follow with nivolumab monotherapy) In combination with pembrolizumab as subsequent therapy: o Administer 1 mg/kg intravenously every 3 weeks for a maximum of 4 doses (given in combination with pembrolizumab, then follow with pembrolizumab monotherapy)
Cutaneous Melanoma (adjuvant therapy)	Administer 10 mg/kg intravenously every 3 weeks for 4 doses, followed by 10 mg/kg intravenously every 12 weeks for up to 3 years
Uveal Melanoma	Single agent: o Administer 3 mg/kg or 10mg/kg intravenously every 3 weeks for 4 doses In combination with nivolumab: o Administer 3 mg/kg intravenously 3 weeks for 4 doses (given in combination with nivolumab, then follow with nivolumab monotherapy)
CNS metastases from melanoma	Single agent: o Initial: Administer 10 mg/kg intravenously every 3 weeks for 4 doses o Subsequent (starting at week 24): Administer 10 mg/kg intravenously every 12 weeks until disease progression or unacceptable toxicity In combination with nivolumab: o Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with nivolumab, then follow with nivolumab monotherapy)
Hepatocellular Carcinoma (HCC)	Administer 3 mg/kg intravenously every 3 weeks for a total of 4 doses (given in combination with nivolumab, then follow with nivolumab monotherapy)
Non-Small Cell Lung Cancer (NSCLC)	In combination with nivolumab: o Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 2 weeks), until disease progression or unacceptable toxicity for up to 2 years In combination with nivolumab and platinum-doublet chemotherapy: o Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 3 weeks and 2 cycles of histology-based platinum-doublet chemotherapy every 3 weeks), until disease progression or unacceptable toxicity for up to 2 years
Renal Cell Carcinoma (RCC), Small Bowel Adenocarcinoma (SBA)/ Advanced Ampullary Cancer	Administer 1 mg/kg intravenously every 3 weeks for a total of 4 doses (given in combination with nivolumab, then follow with nivolumab monotherapy)
Colorectal Cancer (CRC)	Primary treatment

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

	○ Administer 1 mg/kg intravenously every 6 weeks, with nivolumab every 2 weeks, until disease progression or unacceptable toxicity Disease progression or for disease that remains unresectable after primary treatment ○ Administer 1 mg/kg intravenously every 3 weeks for a total of 4 doses (given in combination with nivolumab, then follow with nivolumab monotherapy)
Malignant Pleural Mesothelioma	Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab) until disease progression or unacceptable toxicity for up to 2 years
** All treatments given for a maximum of 4 doses must be administered within 16 weeks of the first dose.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J9228 – Injection, ipilimumab, 1 mg: 1 billable unit = 1 mg

NDC(s):

- Yervoy 200 mg/40 mL injection (single-dose vial): 00003-2328-xx
- Yervoy 50 mg/10 mL injection (single-dose vial): 00003-2327-xx

VII. References

1. Yervoy [package insert]. Princeton, NJ; Bristol Meyers Squib; May 2021. Accessed July 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) ipilimumab. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2021.
3. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Small Cell Lung Cancer. Version 3.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2021.
4. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Central Nervous System Cancers. Version 1.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network,

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2021.
5. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Malignant Pleural Mesothelioma. Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2021.
6. Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma. N Engl J Med. 2010 Aug 19; 363(8):711-23.
7. Wilgenhof S, Du Four S, Vandenbroucke F, et al. Single-center experience with ipilimumab in an expanded access program for patients with pretreated advanced melanoma. J Immunother. 2013 Apr; 36(3):215-22.
8. Margolin K, Ernstoff MS, Hamid O, et al. Ipilimumab in patients with melanoma and brain metastases: an open-label, phase 2 trial. Lancet Oncol. 2012 May; 13(5):459-65.
9. Antonia SJ, López-Martin JA, Bendell J, et al. Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): a multicentre, open-label, phase 1/2 trial. *Lancet Oncol.* 2016 Jul;17(7):883-895.
10. Tawbi HA, Forsyth PAJ, Algazi AP, et al. Efficacy and safety of nivolumab (NIVO) plus ipilimumab (IPI) in patients with melanoma (MEL) metastatic to the brain: Results of the phase II study CheckMate 204. Journal of Clinical Oncology 35, no. 15_suppl (May 2017) 9507-9507.
11. Long GV, Atkinson V, Menzies AM, et al. A randomized phase II study of nivolumab or nivolumab combined with ipilimumab in patients (pts) with melanoma brain metastases (mets): The Anti-PD1 Brain Collaboration (ABC). Journal of Clinical Oncology 35, no. 15_suppl (May 2017) 9508-9508.
12. Hellmann MD, Ciuleanu TE, Pluzanski A, et al. Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden. N Engl J Med 2018; 378:2093-2104.
13. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
14. Hematology/Oncology Pharmacy Association (2019). *Intravenous Cancer Drug Waste Issue Brief*. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
15. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
16. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Non-Small Cell Lung Cancer. Version 5.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network,

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2021.

17. Eggermont AM, Chiarion-Sileni V, Grob JJ, et al. Adjuvant ipilimumab versus placebo after complete resection of high-risk stage III melanoma (EORTC 18071): a randomised, double-blind, phase 3 trial. Lancet Oncol. 2015 May;16(5):522-30. doi: 10.1016/S1470-2045(15)70122-1. Epub 2015 Mar 31.
18. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. N Engl J Med. 2018 Apr 5;378(14):1277-1290. doi: 10.1056/NEJMoa1712126. Epub 2018 Mar 21.
19. Overman MJ, Lonardi S, Wong KYM, et al. Durable Clinical Benefit With Nivolumab Plus Ipilimumab in DNA Mismatch Repair-Deficient/Microsatellite Instability-High Metastatic Colorectal Cancer. J Clin Oncol. 2018 Mar 10;36(8):773-779. doi: 10.1200/JCO.2017.76.9901. Epub 2018 Jan 20.
20. Piulats JM, Cruz-Merino LDL, Garcia MTC, et al. Phase II multicenter, single arm, open label study of nivolumab in combination with ipilimumab in untreated patients with metastatic uveal melanoma (GEM1402.NCT02626962). Annals of Oncology, Volume 29, Issue suppl_8, October 2018, mdy289.003, https://doi.org/10.1093/annonc/mdy289.003.
21. Zimmer L, Vaubel J, Mohr P, et al. Phase II DeCOG-study of ipilimumab in pretreated and treatment-naïve patients with metastatic uveal melanoma. PLoS One. 2015 Mar 11;10(3):e0118564. doi: 10.1371/journal.pone.0118564. eCollection 2015.
22. Danielli R, Ridolfi R, Chiarion-Sileni V, et al. Ipilimumab in pretreated patients with metastatic uveal melanoma: safety and clinical efficacy. Cancer Immunol Immunother. 2012 Jan;61(1):41-8. doi: 10.1007/s00262-011-1089-0. Epub 2011 Aug 11.
23. Luke JJ, Callahan MK, Postow MA, et al. Clinical activity of ipilimumab for metastatic uveal melanoma: a retrospective review of the Dana-Farber Cancer Institute, Massachusetts General Hospital, Memorial Sloan-Kettering Cancer Center, and University Hospital of Lausanne experience. Cancer. 2013 Oct 15;119(20):3687-95. doi: 10.1002/cncr.28282. Epub 2013 Aug 2.
24. Hellmann MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus Ipilimumab in Advanced Non-Small-Cell Lung Cancer. N Engl J Med. 2019 Nov 21;381(21):2020-2031. doi: 10.1056/NEJMoa1910231. Epub 2019 Sep 28.
25. Scherpereel A, Mazieres J, Greillier L, et al. Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial. Lancet Oncol. 2019 Feb;20(2):239-253. doi: 10.1016/S1470-2045(18)30765-4. Epub 2019 Jan 16.
26. Disselhorst MJ, Quispel-Janssen J, Lalezari F, et al. Ipilimumab and nivolumab in the treatment of recurrent malignant pleural mesothelioma (INITIATE): results of a prospective, single-arm, phase 2 trial. Lancet Respir Med. 2019 Mar;7(3):260-270. doi: 10.1016/S2213-2600(18)30420-X. Epub 2019 Jan 16.

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

27. Long GV, Atkinson V, Lo S, et al. Combination nivolumab and ipilimumab or nivolumab alone in melanoma brain metastases: a multicentre randomised phase 2 study. Lancet Oncol. 2018 May;19(5):672-681. doi: 10.1016/S1470-2045(18)30139-6. Epub 2018 Mar 27.
28. Margolin K, Ernstoff MS, Hamid O, et al. Ipilimumab in patients with melanoma and brain metastases: an open-label, phase 2 trial. Lancet Oncol. 2012 May;13(5):459-65. doi: 10.1016/S1470-2045(12)70090-6. Epub 2012 Mar 27.
29. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Small Bowel Adenocarcinoma. Version 1.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2021.
30. El-Khoueiry AB, Sangro B, Yau T, et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial. Lancet. 2017 Jun 24;389(10088):2492-2502. doi: 10.1016/S0140-6736(17)31046-2. Epub 2017 Apr 20.
31. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Colon Cancer. Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2021.
32. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Melanoma: Uveal. Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2021.
33. Hellmann M, Ott PA, Zugazagoitia J, et al. Nivolumab (nivo) ± ipilimumab (ipi) in advanced small-cell lung cancer (SCLC): First report of a randomized expansion cohort from CheckMate 032. J Clin Oncol 2017; 35 Abstract 8503.
34. Zalcman G, Mazieres J, Greillier L, et al. Second- or third-line nivolumab (Nivo) versus nivo plus ipilimumab (Ipi) in malignant pleural mesothelioma (MPM) patients: Updated results of the IFCT-1501 MAPS2 randomized phase 2 trial [abstract]. Ann Oncol 2017; 28:Abstract LBA58_PR.
35. Hellmann MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus Ipilimumab in Advanced Non-Small-Cell Lung Cancer. N Engl J Med. 2019;381(21):2020-2031. doi:10.1056/NEJMoa1910231.
36. Reck M, Ciuleanu T-E, Dols MC, et al. Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx)

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA [abstract]. J Clin Oncol 2020;38:Abstract 9501-9501.
37. Zalcman G, Peters S, Mansfield AS, et al. Checkmate 743: A phase 3, randomized, open-label trial of nivolumab (nivo) plus ipilimumab (ipi) vs pemetrexed plus cisplatin or carboplatin as first-line therapy in unresectable pleural mesothelioma. Journal of Clinical Oncology 2017 35:15_suppl, TPS8581-TPS8581.
38. Olson D, Luke J, Poklepovic A, et al. Significant antitumor activity for low-dose ipilimumab (IPI) with pembrolizumab (PEMBRO) immediately following progression on PD1 Ab in melanoma (MEL) in a phase II trial. Journal of Clinical Oncology 2020 38:15_suppl, 10004-10004
39. Pelster MS, Gruschkus SK, Bassett R, et al. Nivolumab and Ipilimumab in Metastatic Uveal Melanoma: Results From a Single-Arm Phase II Study. J Clin Oncol. 2021 Feb 20;39(6):599-607. doi: 10.1200/JCO.20.00605.
40. Carlino MS, Menzies AM, Atkinson V, et al. Long-term Follow-up of Standard-Dose Pembrolizumab Plus Reduced-Dose Ipilimumab in Patients with Advanced Melanoma: KEYNOTE-029 Part 1B. Clin Cancer Res. 2020 Oct 1;26(19):5086-5091. doi: 10.1158/1078-0432.CCR-20-0177.
41. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. N Engl J Med. 2015 Jul 2;373(1):23-34. doi: 10.1056/NEJMoa1504030. Epub 2015 May 31.
42. Lenz HJ, Lonardi S, Zagonel V, et al. Nivolumab (NIVO) + low-dose ipilimumab (IPI) as first-line (1L) therapy in microsatellite instability-high/DNA mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Clinical update [abstract]. Journal of Clinical Oncology 2019;37:3521-3521.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

ICD-10	ICD-10 Description
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.0	Liver cell carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C24.1	Malignant neoplasm of ampulla of Vater
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C38.4	Malignant neoplasm of pleura
C43.0	Malignant melanoma of lip
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.11	Malignant melanoma of right eyelid, including canthus
C43.12	Malignant melanoma of left eyelid, including canthus
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

ICD-10	ICD-10 Description
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C45.0	Mesothelioma of pleura
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C69.30	Malignant neoplasm of unspecified choroid
C69.31	Malignant neoplasm of right choroid
C69.32	Malignant neoplasm of left choroid
C69.40	Malignant neoplasm of unspecified ciliary body
C69.41	Malignant neoplasm of right ciliary body
C69.42	Malignant neoplasm of left ciliary body
C69.60	Malignant neoplasm of unspecified orbit
C69.61	Malignant neoplasm of right orbit
C69.62	Malignant neoplasm of left orbit
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.31	Secondary malignant neoplasm of brain
Z85.038	Personal history of other malignant neoplasm of large intestine

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

ICD-10	ICD-10 Description
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.820	Personal history of malignant melanoma of skin

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management