

Yervoy™ (ipilimumab) (Intravenous)

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I. Length of Authorization

Small and Non-Small Cell Lung Cancer (SCLC/NSCLC)/Renal Cell Carcinoma (RCC)/Melanoma (unresectable or metastatic)/Colorectal Cancer (CRC)

- Coverage will be provided for 12 weeks (may be extended to 16 weeks if 4 doses were not administered within the 12 week time frame) and may not be renewed (*unless the patient meets the provisions for metastatic or unresectable melanoma re-induction*).

Melanoma (maintenance adjuvant therapy)

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

CNS metastases from Melanoma

- Coverage will be provided for 12 weeks initially (may be extended to 16 weeks if 4 doses were not administered within the 12 week time frame). Coverage may be renewed in 6 month intervals thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- 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)

B. Max Units (per dose and over time) [Medical Benefit]:

- **Unresectable or metastatic Melanoma**
 - 350 billable units per 21 days x 4 doses
- **Adjuvant treatment of Melanoma**
 - 1150 billable units per 21 days x 4 doses; then 1150 billable units per 84 days

- **CNS metastases from Melanoma**
 - Initial authorization: 1150 billable units per 21 days x 4 doses
 - Subsequent authorizations: 1150 billable units per 84 days
- **Colorectal Cancer (CRC)**
 - 115 billable units per 21 days x 4 doses
- **Renal Cell Carcinoma (RCC)**
 - 115 billable units per 21 days x 4 doses
- **Small Cell Lung Cancer (SCLC)/Non-Small Cell Lung Cancer (NSCLC)**
 - 350 billable units per 21 days x 4 doses

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is 18 years or older, unless otherwise indicated; **AND**

Melanoma †

- Patient's disease is unresectable or metastatic; **AND**
 - Used as a single agent in patients 12 years or older †; **OR**
 - Used in combination with nivolumab; **OR**
 - Used for retreatment of disease as re-induction or subsequent therapy (*see Section IV for criteria*); **OR**
- Ipilimumab will be used as adjuvant treatment; **AND**
 - Used as a single agent; **AND**
 - Patient has cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm and has undergone complete resection including total lymphadenectomy †; **OR**
 - Following complete lymph node dissection and/or complete resection of nodal recurrence †; **OR**
 - Following complete resection of distant metastatic disease in patients with cutaneous melanoma †; **OR**
- Used as a single agent or in combination with nivolumab for unresectable or metastatic Uveal Melanoma ‡

Renal Cell Carcinoma (RCC) †

- Used as initial therapy in combination with nivolumab; **AND**
 - Patient has advanced or metastatic disease with intermediate or poor risk; **OR**
- Used as subsequent therapy in combination with nivolumab ‡; **AND**
 - Patient has relapsed or surgically unresectable stage IV disease; **AND**
 - Used for predominant clear cell histology

Small Cell Lung Cancer (SCLC) ‡

- Used as subsequent therapy in combination with nivolumab; **AND**
- Patient's performance status (ECOG) score is 0-2; **AND**
 - Used for primary progressive disease; **OR**
 - Used for relapse within 6 months of initial therapy following a complete or partial response or stable disease

Non-Small Cell Lung Cancer (NSCLC) ‡

- Used in combination with nivolumab; **AND**
- Patient has disease with a high tumor mutational burden (TMB) (i.e., ≥ 10 mutations per megabase)

Central nervous system cancers ‡

- Patient must have brain metastases from melanoma; **AND**
- Ipilimumab must have been active against the primary melanoma tumor; **AND**
 - Used as initial therapy in combination with nivolumab; **OR**
 - Used for recurrent disease as a single agent or in combination with nivolumab

Microsatellite Instability-High (MSI-H)/Mismatch Repair Deficient (dMMR) Colorectal Cancer †

- Patient must be at least 12 years of age; **AND**
- Used in combination with nivolumab; **AND**
- Patient's disease must be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); **AND**
 - Patient has unresectable advanced or metastatic disease that has progressed following a fluoropyrimidine-oxaliplatin, and/or irinotecan regimen; **OR**
 - Used as primary treatment for metastatic disease after adjuvant therapy with a fluoropyrimidine and oxaliplatin regimen within the past 12 months

† FDA approved indication(s); ‡ Compendia recommended indication

IV. Renewal Criteria

- Patient continues to meet the criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: immune-mediated reactions (e.g. enterocolitis, hepatitis, dermatitis, neuropathies, endocrinopathies like hypopituitarism, hypothyroidism, hypogonadism, or adrenal insufficiency, and ocular disease, etc); **AND**

Melanoma (metastatic or unresectable disease) ‡

- Patient has completed initial induction (completion of 4 cycles within a 16 week period); **AND**

- Used as re-induction therapy in patients who experienced disease control (i.e, complete or partial response or stable disease), but subsequently disease progression/relapse > 3 months after treatment discontinuation; **OR**
- Used as subsequent therapy, in combination with nivolumab, in patients who experienced disease relapse and/or progression within 3 months after initial monotherapy with an immune checkpoint-inhibitor

Melanoma Maintenance therapy (adjuvant treatment)

- Tumor response/absence of recurrence; **AND**
- Length of therapy has not exceeded 3 years

CNS metastases from melanoma

- Initial renewal: Patient’s disease is clinically stable at week 24
- Subsequent renewals: Tumor response/absence of recurrence

Small Cell Lung Cancer (SCLC)/Renal Cell Carcinoma (RCC)

- Coverage may not be renewed.

V. Dosage/Administration

Indication	Dose
Melanoma (unresectable or metastatic)	3 mg/kg every 3 weeks for a total of 4 doses * <i>all treatment must be administered within 16 weeks of the first dose</i>
Melanoma (adjuvant)	10 mg/kg every 3 weeks for 4 doses, followed by 10 mg/kg every 12 weeks for up to 3 years
CNS metastases from melanoma	<p><u>Single Agent</u></p> <ul style="list-style-type: none"> - <u>Initial</u>: 10 mg/kg every 3 weeks for 4 doses - <u>Subsequent</u>: 10 mg/kg every 12 weeks <p><u>Combination Therapy (with nivolumab)</u></p> <ul style="list-style-type: none"> - <u>Initial</u>: Ipilimumab 3 mg/kg and Nivolumab 1mg/kg every 3 weeks for 4 doses - <u>Subsequent</u>: Nivolumab 3 mg/kg every 2 weeks until disease progression or intolerance
Small Cell Lung Cancer (SCLC), Non-Small Cell Lung Cancer (NSCLC)	3 mg/kg every 3 weeks for a total of 4 doses (given in combination with nivolumab followed by nivolumab monotherapy) * <i>all treatment must be administered within 16 weeks of the first dose</i>
Renal Cell Carcinoma (RCC) and Colorectal Cancer (CRC)	1 mg/kg every 3 weeks for a total of 4 doses (given in combination with nivolumab followed by nivolumab monotherapy)

VI. Billing Code/Availability Information

JCode:

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

NDC(s):

- Yervoy 200 mg/40 mL injection: 00003-2328-xx
- Yervoy 50 mg/10 mL injection: 0003-2327-xx

VII. References

1. Yervoy [package insert]. Princeton, NJ; Bristol Meyers Squib; July 2018. Accessed November 2018.
2. Opdivo [package insert]. Princeton, NJ; Bristol-Myers Squibb Company; August 2018. Accessed November 2018.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) ipilimumab. National Comprehensive Cancer Network, 2018. 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 November 2018.
4. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Small Cell Lung Cancer. National Comprehensive Cancer Network, Version 1.2019. 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 November 2018.
5. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Central Nervous System Cancers. National Comprehensive Cancer Network, Version 1.2018. 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 November 2018.
6. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Malignant Pleural Mesothelioma. National Comprehensive Cancer Network, Version 2.2018. 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 November 2018.
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9. 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.
10. 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
11. 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.
12. 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.
13. 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.

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
C17.8	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
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
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

ICD-10	ICD-10 Description
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
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
C43.20	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
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
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

YERVOY™ (ipilimumab) Prior Auth Criteria

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ICD-10	ICD-10 Description
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
C69.90	Malignant neoplasm of unspecified site of unspecified eye
C69.91	Malignant neoplasm of unspecified site of right eye
C69.92	Malignant neoplasm of unspecified site of left eye
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
C79.51	Secondary malignant neoplasm of bone
C79.52	Secondary malignant neoplasm of bone marrow
C7A.1	Malignant poorly differentiated neuroendocrine tumors
C80.0	Disseminated malignant neoplasm, unspecified
C80.1	Malignant (primary) neoplasm, unspecified
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.528	Personal history of other malignant neoplasm of kidney
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) and Local Coverage Determinations (LCDs) 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): 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