

Yervoy® (ipilimumab) (Intravenous)

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I. Length of Authorization ^Δ 1,5,6,8-12,17-19,20,24,27-29,31,33,39-42,44,46-49,53,54

Coverage will be provided for 6 months and may be renewed (unless otherwise specified).

- The following indications may be authorized up to a maximum of 12 weeks of therapy (4 doses) 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 (*subsequent therapy*)
 - CNS metastases from Melanoma (*combination therapy with nivolumab*)
 - Hepatocellular Carcinoma
 - Renal Cell Carcinoma
 - Cutaneous Melanoma (*first-line or subsequent therapy*)
 - * *Requests for Cutaneous Melanoma may be renewed if the patient meets the provisions for re-induction therapy.*
 - Cutaneous Melanoma (*adjuvant therapy in combination with nivolumab*)
 - Uveal Melanoma
- The following indications may be renewed up to a maximum of 2 years of therapy (18 doses):
 - Biliary Tract Cancer
 - Bone Cancer
 - Esophageal and Esophagogastric/Gastroesophageal Junction Cancer (*first-line therapy for disease that is NOT MSI-H/dMMR*)
 - Kaposi Sarcoma
 - Malignant Pleural Mesothelioma (*initial therapy*)
 - Non-Small Cell Lung Cancer

MSI-H/dMMR Gastric, Esophageal, and Esophagogastric/Gastroesophageal Junction Cancer (*Neoadjuvant or Perioperative Therapy*)

- Coverage will be provided for a maximum of 12 weeks of pre-operative therapy (2 doses) and may not be renewed

Cutaneous Melanoma (single agent adjuvant treatment)

- Coverage will be provided for 6 months and may be renewed for up to a maximum of 3 years of maintenance therapy (17 doses total [initial and maintenance doses combined]).

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)

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

Indication	Billable Units (BU)	Per unit time (days)
CNS Cancer, HCC, Cutaneous Melanoma, Uveal Melanoma, & MCC	350 BU	21 days
CNS Cancer, Cutaneous Melanoma, & Uveal Melanoma	1150 BU	21 days
CNS Cancer & Cutaneous Melanoma	1150 BU	84 days
CRC, Cutaneous Melanoma, & RCC	150 BU	21 days
Biliary Tract Cancer, Bone Cancer, CRC, Esophageal and Esophagogastric/Gastroesophageal Junction Cancer, Kaposi Sarcoma, MPM, MCC, NSCLC, & Soft Tissue Sarcoma	150 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**

Biliary Tract Cancers (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma) ‡ 2,46,116e

- Patient has tumor mutational burden-high (TMB-H) ≥ 10 mutations/megabase (mut/Mb) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used as subsequent treatment for progression on or after systemic treatment for unresectable, resected gross residual (R2), or metastatic disease; **AND**
- Used in combination with nivolumab; **AND**
- Disease is refractory to standard therapies or there are no standard treatment options available

Bone Cancer ‡ 2,46,116e

- Patient has one of the following: Ewing sarcoma, Chondrosarcoma (*excluding mesenchymal chondrosarcoma*), Osteosarcoma, or Chordoma; **AND**
- Patient has tumor mutation burden-high (TMB-H) ≥ 10 mutations/megabase (mut/Mb) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used in combination with nivolumab; **AND**
- Patient has unresectable or metastatic disease that progressed following prior treatment; **AND**
- Patient has no satisfactory alternative treatment options

Central Nervous System (CNS) Cancer ‡ 2,4,8,10,11,27,82e

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

Colorectal Cancer (CRC) † ‡ 1,2,19,31,42,85e-87e,94e

- Patient is at least 12 years of age; **AND**
- Patient has microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR) disease OR polymerase epsilon/delta (POLE/POLD1) mutation as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used in combination with nivolumab*; **AND**
 - Used as subsequent therapy; **AND**
 - Patient has metastatic, unresectable, or medically inoperable disease that progressed following treatment with a fluoropyrimidine-, oxaliplatin-, and/or irinotecan-based chemotherapy † ‡; **OR**
 - Used as primary or initial treatment; **AND**
 - Used for isolated pelvic/anastomotic recurrence of rectal cancer; **OR**
 - Patient has T3, N Any; T1-2, N1-2; T4, N Any rectal cancer; **OR**
 - Patient has metastatic, unresectable, or medically inoperable disease

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

Esophageal Cancer and Esophagogastric/Gastroesophageal Junction Cancers † ‡ 1,2,45,53,105e

- Used in combination with nivolumab; **AND**
 - Used as first-line therapy; **AND**
 - Patient has esophageal squamous cell carcinoma †; **AND**
 - Patient is not a surgical candidate or has unresectable advanced, recurrent, or metastatic disease; **OR**
 - Used as neoadjuvant or perioperative therapy; **AND**
 - Patient has esophagogastric/gastroesophageal junction adenocarcinoma; **AND**
 - Used as primary treatment for patients who are medically fit for surgery with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease; **AND**
 - Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖

Gastric Cancer † 2,54

- Used in combination with nivolumab; **AND**
- Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used as neoadjuvant or perioperative therapy; **AND**
- Used as primary treatment prior to surgery for potentially resectable locoregional disease (cT2 or higher, any N) in patients who are medically fit for surgery

Hepatocellular Carcinoma (HCC) † 1,2,30,30e,31e,33e,34e

- Used in combination with nivolumab; **AND**
- Used as subsequent therapy for progressive disease; **AND**
- Patient has Child-Pugh Class A hepatic impairment; **AND**
- Used for one of the following:
 - Patient was previously treated with sorafenib †
 - Patient has unresectable disease and is not a transplant candidate
 - Patient has liver-confined disease that is inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic-disease
 - Patient has metastatic disease or extensive liver tumor burden

Kaposi Sarcoma † 2,47

- Used in combination with nivolumab as subsequent therapy; **AND**
- Patient has classic disease; **AND**
- Used for relapsed/refractory advanced cutaneous, oral, visceral, or nodal disease; **AND**

- Disease progressed on or did not respond to first-line therapy; **AND**
- Disease progressed on alternate first-line therapy

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 poor or intermediate risk advanced, relapsed, or stage IV disease; **OR**
 - Used as first-line therapy in patients with favorable risk relapsed or stage IV disease

Malignant Pleural Mesothelioma (MPM) † ‡ Φ 1,2,5,25,26,34,37

- Used in combination with nivolumab; **AND**
 - Used as subsequent therapy (if platinum chemotherapy was administered first-line); **OR**
 - Used as first-line therapy in patients with medically inoperable or unresectable disease

Cutaneous Melanoma † ‡ Φ 1,2,6,17,43,5e,8e,11e,13e,21e-23e,99e,100e

- Used as first-line therapy for unresectable or metastatic* disease †; **AND**
 - Patient is at least 12 years of age; **AND**
 - Used as a single agent or in combination with nivolumab; **OR**
- Used as subsequent therapy for unresectable or metastatic* disease; **AND**
 - Used after disease progression, intolerance, and/or projected risk of progression with 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 therapy †; **OR**
 - Used in combination with nivolumab in patients at least 12 years of age if not previously used or for patients who progress on single agent anti-PD-1 therapy †; **OR**
 - Used in combination with pembrolizumab if not previously used alone or in combination with anti-PD-1 therapy for patients who progress on single agent anti-PD-1 therapy; **OR**
 - Used as re-induction therapy in patients who experienced disease control (*i.e., complete or partial response or stable disease*) and no residual toxicity from prior use, but subsequently have disease progression/relapse > 3 months after treatment discontinuation; **AND**
 - Used as a single agent; **AND**
 - Patient has completed initial induction ipilimumab therapy (*i.e., completion of 4 cycles within a 16 week period*); **OR**
- Used as adjuvant treatment; **AND**
 - Used as a single agent; **AND**

- Patient has stage III disease with pathologic involvement of regional lymph nodes of more than 1 mm and has undergone complete resection including total lymphadenectomy †; **OR**
- Used in combination with nivolumab; **AND**
 - Patient has oligometastatic disease and no evidence of disease (NED) following metastasis-directed therapy (i.e., complete resection, stereotactic ablative therapy or T-VEC/intralesional therapy) OR following systemic therapy followed by resection
- Used as neoadjuvant therapy; **AND**
 - Used in combination with nivolumab; **AND**
 - Patient has stage III disease; **AND**
 - Used as primary treatment for clinically positive, resectable nodal disease; **OR**
 - Patient has resectable disease limited to nodal recurrence

**Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in-transit metastases, as well as unresectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.*

Uveal Melanoma † ^{2,20-23,32}

- Patient has metastatic or unresectable disease; **AND**
 - Used as a single agent; **OR**
 - Used in combination with nivolumab as first-line therapy

Merkel Cell Carcinoma † ^{2,50,51}

- Used for M1 disseminated disease; **AND**
- Used in combination with nivolumab; **AND**
- Patient progressed on anti-PD-L1 or anti-PD-1 therapy OR anti-PD-L1 or anti-PD-1 therapy is contraindicated

Non-Small Cell Lung Cancer (NSCLC) † ‡ ^{1,2,12,16,24,36,35e-37e,43e,50e,89e,110e}

- 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 a performance status (PS) 0-1 who have tumors that are negative for actionable molecular biomarkers** ‡ and PD-L1 <1%
 - Patients with a PS 0-1 who are positive for one of the following molecular biomarkers: EGFR exon 20, KRAS G12C, BRAF V600E,

NTRK1/2/3 gene fusion, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2)

- PD-L1 expression positive (PD-L1 $\geq 1\%$) tumors, as detected by an FDA or CLIA compliant test \blacklozenge , that are tumors that are negative for actionable molecular biomarkers** \yen ; **AND**
- Used in combination with one of the following:
 - Nivolumab
 - Nivolumab and platinum-doublet chemotherapy (e.g., pemetrexed and either carboplatin or cisplatin for nonsquamous 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 a PS 0-1 who are positive for one of the following molecular biomarkers and have received prior targeted therapy \S : EGFR exon 19 deletion or exon 21 L858R tumors, EGFR S768I, L861Q, and/or G719X, ALK rearrangement, or ROS1 rearrangement
 - Patients with a PS 0-1 who are positive for one of the following molecular biomarkers: BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping, or RET rearrangement; **AND**
 - Used in combination with one of the following:
 - Nivolumab
 - Nivolumab, pemetrexed, and either carboplatin or cisplatin for nonsquamous cell histology
 - 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, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2). Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2) via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.

\yen May also be used for patients with KRAS G12C mutation positive tumors.

Soft Tissue Sarcoma † 2,46,52

- Extremity/Body Wall, Head/Neck* or Retroperitoneal/Intra-Abdominal**
 - Used in combination with nivolumab; **AND**
 - Used as subsequent therapy; **AND**
 - Patient has tumor mutational burden-high (TMB-H) [≥ 10 mutations/megabase (mut/Mb)] disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
 - Patient has no satisfactory alternative treatment options; **OR**
- Pleomorphic Rhabdomyosarcoma
 - Used in combination with nivolumab; **AND**
 - Used as subsequent therapy; **AND**
 - Patient has tumor mutational burden-high (TMB-H) [≥ 10 mutations/megabase (mut/Mb)] disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
 - Patient has no satisfactory alternative treatment options

**For atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLs) of the extremity, abdominal wall, trunk that was initially diagnosed as ALT and shows evidence of de-differentiation, treat as other soft tissue sarcomas.*

***For well-differentiated liposarcoma (WDLs-retroperitoneum, paratesticular) with or without evidence of de-differentiation, treat as other soft tissue sarcomas; risk of WDLs progression without de-differentiation is low and therefore single-agent systemic therapy is recommended.*

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

❖ *If confirmed using an FDA approved assay – <http://www.fda.gov/CompanionDiagnostics>*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication; Ⓢ Orphan Drug

§ Genomic Aberration/Mutational Driver Targeted Therapies			
(Note: not all inclusive, refer to guidelines for appropriate use)			
EGFR exon 19 deletion or exon 21 L858R tumors	EGFR S768I, L861Q, and/or G719X mutation positive tumors	EGFR exon 20 insertion mutation positive tumors	NTRK1/2/3 gene fusion positive tumors
<ul style="list-style-type: none"> – Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab 	<ul style="list-style-type: none"> – Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab 	<ul style="list-style-type: none"> – Amivantamab 	<ul style="list-style-type: none"> – Larotrectinib – Entrectinib
ALK rearrangement-positive tumors	ROS1 rearrangement-positive tumors	BRAF V600E-mutation positive tumors	ERBB2 (HER2) mutation positive tumors
<ul style="list-style-type: none"> – Alectinib – Brigatinib – Ceritinib 	<ul style="list-style-type: none"> – Ceritinib – Crizotinib – Entrectinib 	<ul style="list-style-type: none"> – Dabrafenib ± trametinib – Encorafenib + binimetinib – Vemurafenib 	<ul style="list-style-type: none"> – Fam-trastuzumab – deruxtecan-nxki – Ado-trastuzumab emtansine

– Crizotinib – Lorlatinib	– Lorlatinib – Repotrectinib		
PD-L1 tumor expression \geq 1%	<i>MET</i> exon-14 skipping mutations	<i>RET</i> rearrangement-positive tumors	<i>KRAS G12C</i> mutation positive tumors
– Pembrolizumab – Atezolizumab – Nivolumab + ipilimumab – Cemiplimab – Tremelimumab + durvalumab	– Capmatinib – Crizotinib – Tepotinib	– Selpercatinib – Cabozantinib – Pralsetinib	– Sotorasib – Adagrasib

IV. Renewal Criteria ^{Δ 1,2,6,9-12,17-29,39-41,46-49,53,54}

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the 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: severe immune-mediated adverse reactions (e.g., colitis, hepatitis, dermatitis/rash, pneumonitis, nephritis/renal dysfunction, endocrinopathies, etc.), severe infusion-related reactions, complications of allogeneic hematopoietic stem cell transplantation (HSCT), 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:
 - Colorectal Cancer (*subsequent therapy*)
 - CNS metastases from Melanoma (*combination therapy with nivolumab*)
 - MSI-H/dMMR Gastric, Esophageal, and Esophagogastric/Gastroesophageal Junction Cancer
 - Hepatocellular Carcinoma
 - Renal Cell Carcinoma
 - Cutaneous Melanoma (*first-line or subsequent therapy*)
 - * *Requests for Cutaneous Melanoma may be renewed if the patient meets the provisions for re-induction therapy (see below).*
 - Cutaneous Melanoma (*adjuvant therapy in combination with nivolumab*)
 - Uveal Melanoma
- For the following indications, patient has not exceeded a maximum of 2 years of therapy (18 doses):
 - Biliary Tract Cancer
 - Bone Cancer
 - Esophageal and Esophagogastric/Gastroesophageal Junction Cancer (*first-line therapy for disease that is NOT MSI-H/dMMR*)

- Kaposi Sarcoma
- Malignant Pleural Mesothelioma (*initial therapy*)
- Non-Small Cell Lung Cancer

Cutaneous Melanoma (re-induction therapy) ‡

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

Cutaneous Melanoma (single agent adjuvant treatment – maintenance therapy)

- Patient has not exceeded a maximum of 3 years of therapy (17 doses total [initial and maintenance doses combined])

Non-Small Cell Lung Cancer (continuation maintenance therapy)

- *Refer to Section III for criteria*

<p>^Δ <u>Notes:</u></p> <ul style="list-style-type: none"> • Patients responding to therapy who relapse ≥ 6 months after discontinuation due to duration (i.e., receipt of 24 months of PD-directed therapy) are eligible to re-initiate checkpoint inhibitor therapy. • Patients who complete adjuvant therapy and progress ≥ 6 months after discontinuation are eligible to re-initiate checkpoint inhibitor therapy for metastatic disease. • Patients whose tumors, upon re-biopsy, demonstrate a change in actionable mutation (e.g., MSS initial biopsy; MSI-H subsequent biopsy) may be eligible to re-initiate checkpoint inhibitor therapy and will be evaluated on a case-by-case basis. 	
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V. Dosage/Administration ^{Δ 1,5,6,8-12,17-29,31,33,34,38-42,44,46-55}

Indication	Dose
Renal Cell Carcinoma (RCC)	Administer 1 mg/kg intravenously every 3 weeks for a total of 4 doses (given in combination with nivolumab on the same day, then follow with nivolumab monotherapy)
Biliary Tract Cancers, Bone Cancer, & Kaposi Sarcoma	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 24 months (2 years)
CNS Cancers	<p><u>Single agent:</u></p> <ul style="list-style-type: none"> ○ <u>Initial:</u> Administer 10 mg/kg intravenously every 3 weeks for 4 doses ○ <u>Subsequent (starting at week 24):</u> Administer 10 mg/kg intravenously every 12 weeks until disease progression or unacceptable toxicity <p><u>In combination with nivolumab:</u></p>

	<ul style="list-style-type: none"> Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with nivolumab on the same day, then follow with nivolumab monotherapy)
Colorectal Cancer (CRC)	<p><u>Primary/initial treatment</u></p> <ul style="list-style-type: none"> Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 2 weeks), until disease progression or unacceptable toxicity <p><u>Subsequent therapy</u></p> <ul style="list-style-type: none"> Administer 1 mg/kg intravenously every 3 weeks for a total of 4 doses (given in combination with nivolumab on the same day, then follow with nivolumab monotherapy)
Esophageal and Esophagogastric/Gastroesophageal Junction Cancer	Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 2 or 3 weeks) until disease progression or unacceptable toxicity for up to 2 years
MSI-H/dMMR Gastric, Esophageal, and Esophagogastric/Gastroesophageal Junction Cancer	<p><u>Neoadjuvant/pre-operative therapy:</u></p> <ul style="list-style-type: none"> Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 2 weeks) for 12 weeks, followed by surgery and then postoperative therapy with nivolumab
Hepatocellular Carcinoma (HCC)	Administer 3 mg/kg intravenously every 3 weeks for a total of 4 doses (given in combination with nivolumab on the same day, then follow with nivolumab monotherapy)
Malignant Pleural Mesothelioma (MPM)	<p><u>Initial therapy</u></p> <ul style="list-style-type: none"> Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 2 or 3 weeks) until disease progression or unacceptable toxicity for up to 2 years <p><u>Subsequent therapy</u></p> <ul style="list-style-type: none"> Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 2 weeks) until disease progression or unacceptable toxicity
Cutaneous Melanoma (<i>excluding adjuvant therapy</i>)	<p><u>Single agent or in combination with nivolumab:</u></p> <ul style="list-style-type: none"> Administer 3 mg/kg intravenously every 3 weeks for a maximum of 4 doses (when given in combination with nivolumab on the same day, follow with nivolumab monotherapy) <p><u>In combination with pembrolizumab as subsequent therapy:</u></p> <ul style="list-style-type: none"> Administer 1 mg/kg intravenously every 3 weeks for a maximum of 4 doses (given in combination with pembrolizumab on the same day, then follow with pembrolizumab monotherapy)
Cutaneous Melanoma (adjuvant therapy)	<p><u>Single agent</u></p> <ul style="list-style-type: none"> <u>Initial:</u> Administer 10 mg/kg intravenously every 3 weeks for up to a maximum of 4 doses <u>Maintenance:</u> Administer 10 mg/kg intravenously every 12 weeks for up to 3 years <p><u>In combination with nivolumab</u></p>

	<ul style="list-style-type: none"> Administer 3 mg/kg intravenously every 3 weeks for a maximum of 4 doses (given in combination with nivolumab on the same day)
Uveal Melanoma	<p><u>Single agent:</u></p> <ul style="list-style-type: none"> Administer 3 mg/kg or 10mg/kg intravenously every 3 weeks for 4 doses <p><u>In combination with nivolumab:</u></p> <ul style="list-style-type: none"> Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with nivolumab on the same day, then follow with nivolumab monotherapy)
Merkel Cell Carcinoma	<p>Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 2 weeks) until disease progression or unacceptable toxicity</p> <p>OR</p> <p>Administer 3 mg/kg intravenously every 3 weeks for a maximum of 4 doses (given with nivolumab every 3 weeks, may follow with nivolumab monotherapy)</p>
Non-Small Cell Lung Cancer (NSCLC)	<p><u>In combination with nivolumab:</u></p> <ul style="list-style-type: none"> Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 3 weeks), until disease progression or unacceptable toxicity for up to 2 years <p><u>In combination with nivolumab and platinum-doublet chemotherapy:</u></p> <ul style="list-style-type: none"> Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 3 weeks and histology-based platinum-doublet chemotherapy every 3 weeks for 2 cycles) until disease progression or unacceptable toxicity for up to 2 years
Soft Tissue Sarcoma	Administer 1 mg/kg intravenously every 6 weeks (given in combination with nivolumab every 2 weeks) until disease progression or unacceptable toxicity
* 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 50 mg/10 mL injection (single-dose vial): 00003-2327-xx
- Yervoy 200 mg/40 mL injection (single-dose vial): 00003-2328-xx

VII. References (STANDARD)

- Yervoy [package insert]. Princeton, NJ; Bristol Meyers Squib; February 2023. Accessed March 2024.
- Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) ipilimumab. National Comprehensive Cancer Network, 2024. 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 March 2024.

3. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Small Cell Lung Cancer. Version 2.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
4. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Central Nervous System Cancers. Version 1.2023. National Comprehensive Cancer Network, 2024. 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 March 2024.
5. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Mesothelioma: Pleural. Version 1.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
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 22024. National Comprehensive Cancer Network, 2024. 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 March 2024.
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.
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 2.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
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 1.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
32. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Melanoma: Uveal. Version 1.2023. National Comprehensive Cancer Network, 2024. 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 March 2024.

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) 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.
43. Hodi FS, Chiarion-Sileni V, Gonzalez R, et al. Nivolumab plus ipilimumab or nivolumab alone versus ipilimumab alone in advanced melanoma (CheckMate 067): 4-year outcomes of

- a multicentre, randomised, phase 3 trial. *Lancet Oncol.* 2018 Nov;19(11):1480-1492. doi: 10.1016/S1470-2045(18)30700-9. Epub 2018 Oct 22. Erratum in: *Lancet Oncol.* 2018 Dec;19(12):e668. Erratum in: *Lancet Oncol.* 2018 Nov;19(11):e581.
44. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Mesothelioma: Peritoneal. Version 1.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
 45. Doki Y, Ajani JA, Kato K, et al. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. *N Engl J Med.* 2022 Feb 3;386(5):449-462. doi: 10.1056/NEJMoa2111380.
 46. Schenker M, Burotto M, Richardet M, et al. CheckMate 848: A randomized, open-label, phase 2 study of nivolumab in combination with ipilimumab or nivolumab monotherapy in patients with advanced or metastatic solid tumors of high tumor mutational burden. Oral Presentation presented at the American Association for Cancer Research (AACR) 2022 Annual Meeting; April 8-13, 2022; New Orleans, LA.
 47. Zer A, Icht O, Yosef L, et al. Phase II single-arm study of nivolumab and ipilimumab (Nivo/Ipi) in previously treated classical Kaposi sarcoma (cKS). *Annals of Oncology.* Volume 33, Issue 7, July 2022, Pages 720-727. <https://doi.org/10.1016/j.annonc.2022.03.012>.
 48. Blank CU, Rozeman EA, Fanchi LF, et al. Neoadjuvant versus adjuvant ipilimumab plus nivolumab in macroscopic stage III melanoma. *Nat Med.* 2018 Nov;24(11):1655-1661. doi: 10.1038/s41591-018-0198-0.
 49. Baas P, Scherpereel A, Nowak AK, et al. First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): a multicentre, randomised, open-label, phase 3 trial. *Lancet.* 2021 Jan 30;397(10272):375-386. doi: 10.1016/S0140-6736(20)32714-8.
 50. Glutsch V, Kneitz, Gesierich A, et al. Activity of ipilimumab plus nivolumab in avelumab-refractory Merkel cell carcinoma. *Cancer Immunology, Immunotherapy* volume 70, pages2087–2093 (2021)
 51. Kim S, Wuthrick E, Blakaj D, et al. Combined nivolumab and ipilimumab with or without stereotactic body radiation therapy for advanced Merkel cell carcinoma: a 17 randomized, open label, phase 2 trial. *The Lancet.* Published: September 11, 2022. doi:[https://doi.org/10.1016/S0140-6736\(22\)01659-2](https://doi.org/10.1016/S0140-6736(22)01659-2). PlumX Metrics
 52. Wagner M, Othus M, Patel S, et al. Multicenter phase II trial (SWOG S1609, cohort 51) of ipilimumab and nivolumab in metastatic or unresectable angiosarcoma: a substudy of dual anti-CTLA-4 and anti-PD-1 blockade in rare tumors (DART). *J Immunother Cancer.* 2021 Aug;9(8):e002990. doi: 10.1136/jitc-2021-002990.
 53. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Esophageal and Esophagogastric Junction Cancers. Version 4.2023. National

Comprehensive Cancer Network, 2024. 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 March 2024.

54. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Gastric Cancer. Version 3.2023. National Comprehensive Cancer Network, 2024. 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 March 2024.
55. LoPiccolo J, Schollenberger MD, Dakhil S, et al. Rescue therapy for patients with anti-PD-1-refractory Merkel cell carcinoma: a multicenter, retrospective case series. *J Immunother Cancer*. 2019 Jul 8;7(1):170. doi: 10.1186/s40425-019-0661-6.
56. Dagogo-Jack I, Madison RW, Lennerz JK, et al. Molecular characterization of mesothelioma: Impact of histologic type and site of origin on molecular landscape. *JCO Precis Oncol* 2022;6:e2100422.

VIII. References (ENHANCED)

- 1e. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Melanoma: Cutaneous, Version 1.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
- 2e. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Hepatocellular Carcinoma, Version 2.2023. National Comprehensive Cancer Network, 2024. 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 March 2024.
- 3e. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Kidney Cancer, Version 2.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
- 4e. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Rectal Cancer, Version 1.2024. National Comprehensive Cancer Network,

2024. 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 March 2024.

- 5e. Robert C, Schachter J, Long GV, et al. Pembrolizumab versus Ipilimumab in Advanced Melanoma. *N Engl J Med*. 2015 Jun 25;372(26):2521-32. doi: 10.1056/NEJMoa1503093.
- 6e. Robert C, Long GV, Brady B, et al. Nivolumab in previously untreated melanoma without BRAF mutation. *N Engl J Med*. 2015 Jan 22;372(4):320-30. doi: 10.1056/NEJMoa1412082.
- 7e. Ascierto PA, Long GV, Robert C, et al. Survival Outcomes in Patients With Previously Untreated BRAF Wild-Type Advanced Melanoma Treated With Nivolumab Therapy: Three-Year Follow-up of a Randomized Phase 3 Trial [published correction appears in *JAMA Oncol*. 2019 Feb 1;5(2):271]. *JAMA Oncol*. 2019;5(2):187–194. doi:10.1001/jamaoncol.2018.4514.
- 8e. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma [published correction appears in *N Engl J Med*. 2018 Nov 29;379(22):2185]. *N Engl J Med*. 2015;373(1):23–34. doi:10.1056/NEJMoa1504030.
- 9e. Wolchok JD, Chiarion-Sileni V, Gonzalez R, et al. Overall Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma [published correction appears in *N Engl J Med*. 2018 Nov 29;379(22):2185]. *N Engl J Med*. 2017;377(14):1345–1356. doi:10.1056/NEJMoa1709684.
- 10e. Regan MM, Werner L, Rao S, et al. Treatment-Free Survival: A Novel Outcome Measure of the Effects of Immune Checkpoint Inhibition-A Pooled Analysis of Patients With Advanced Melanoma. *J Clin Oncol*. 2019;37(35):3350-3358. doi:10.1200/JCO.19.00345.
- 11e. Ribas A, Puzanov I, Dummer R, et al. Pembrolizumab versus investigator-choice chemotherapy for ipilimumab-refractory melanoma (KEYNOTE-002): a randomised, controlled, phase 2 trial. *Lancet Oncol*. 2015 Aug;16(8):908-18. doi: 10.1016/S1470-2045(15)00083-2.
- 12e. Hamid O, Puzanov I, Dummer R, et al. Final analysis of a randomised trial comparing pembrolizumab versus investigator-choice chemotherapy for ipilimumab-refractory advanced melanoma. *Eur J Cancer*. 2017 Nov;86:37-45. doi: 10.1016/j.ejca.2017.07.022.
- 13e. Larkin J, Minor D, D'Angelo S, et al. Overall Survival in Patients With Advanced Melanoma Who Received Nivolumab Versus Investigator's Choice Chemotherapy in CheckMate 037: A Randomized, Controlled, Open-Label Phase III Trial. *J Clin Oncol*. 2018;36(4):383–390. doi:10.1200/JCO.2016.71.8023.
- 14e. Hersh EM, O'Day SJ, Ribas A, et al. A phase 2 clinical trial of nab-paclitaxel in previously treated and chemotherapy-naïve patients with metastatic melanoma. *Cancer*. 2010 Jan 1;116(1):155-63.
- 15e. Kottschade LA, Suman VJ, Amatruda T 3rd, et al. A phase II trial of nab-paclitaxel (ABI-007) and carboplatin in patients with unresectable stage IV melanoma: a North Central Cancer Treatment Group Study, N057E(1). *Cancer*. 2011 Apr 15;117(8):1704-10.

- 16e. Agarwala SS, et al. Randomized phase III study of paclitaxel plus carboplatin with or without sorafenib as second-line treatment in patients with advanced melanoma. *Journal of Clinical Oncology* 2007 25:18_suppl, 8510-8510.
- 17e. Rao RD, et al. Combination of paclitaxel and carboplatin as second-line therapy for patients with metastatic melanoma. *Cancer*. 2006 Jan 15;106(2):375-82.
- 18e. Middleton MR, et al. Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. *J Clin Oncol*. 2000 Jan;18(1):158-66.
- 19e. Einzig AI, et al. A phase II study of taxol in patients with malignant melanoma. *Invest New Drugs*. 1991 Feb;9(1):59-64.
- 20e. Robert C, Ribas A, Schachter J, et al. Pembrolizumab versus ipilimumab in advanced melanoma (KEYNOTE-006): post-hoc 5-year results from an open-label, multicentre, randomised, controlled, phase 3 study. *Lancet Oncol* 2019; 20:1239.
- 21e. Eggermont AMM, Blank CU, Mandala M, et al. Adjuvant Pembrolizumab versus Placebo in Resected Stage III Melanoma. *N Engl J Med*. 2018 May 10;378(19):1789-1801. doi: 10.1056/NEJMoa1802357.
- 22e. Eggermont AM, Chiarion-Sileni V, Grob JJ, et al. Prolonged Survival in Stage III Melanoma with Ipilimumab Adjuvant Therapy [published correction appears in *N Engl J Med*. 2018 Nov 29;379(22):2185]. *N Engl J Med*. 2016;375(19):1845–1855. doi:10.1056/NEJMoa1611299.
- 23e. Weber J, Mandala M, Del Vecchio M, et al. Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma. *N Engl J Med*. 2017 Nov 9;377(19):1824-1835. doi: 10.1056/NEJMoa1709030.
- 24e. Kottschade LA, McWilliams RR, Markovic SN, et al. The use of pembrolizumab for the treatment of metastatic uveal melanoma. *Melanoma Res*. 2016 Jun;26(3):300-3. doi: 10.1097/CMR.0000000000000242.
- 25e. Algazi AP, Tsai KK, Shoushtari AN, et al. Clinical outcomes in metastatic uveal melanoma treated with PD-1 and PD-L1 antibodies. *Cancer*. 2016;122(21):3344–3353. doi:10.1002/cncr.30258.
- 26e. Piulats Rodriguez JM, Ochoa de Olza M, Codes M, et al. Phase II study evaluating ipilimumab as a single agent in the first-line treatment of adult patients (Pts) with metastatic uveal melanoma (MUM): The GEM-1 trial. *J Clin Oncol* 2014; 32S:ASCO #9033.
- 27e. Zhu AX, Finn RS, Edeline J, et al. Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224): a non-randomised, open-label phase 2 trial. *Lancet Oncol*. 2018 Jul;19(7):940-952. doi: 10.1016/S1470-2045(18)30351-6.
- 28e. Crocenzi TS, El-Khoueiry AB, Yau T, et al. Nivolumab (nivo) in sorafenib (sor)-naive and -experienced pts with advanced hepatocellular carcinoma (HCC): CheckMate 040 study. *J Clin Oncol* 35, 2017 (suppl; abstr 4013).

- 29e. Qin S, Bai Y, Lim HY, et al. Randomized, multicenter, open-label study of oxaliplatin plus fluorouracil/leucovorin versus doxorubicin as palliative chemotherapy in patients with advanced hepatocellular carcinoma from Asia. *J Clin Oncol*. 2013 Oct 1;31(28):3501-8. doi: 10.1200/JCO.2012.44.5643.
- 30e. Bruix J, Qin S, Merle P, et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2017 Jan 7;389(10064):56-66.
- 31e. Abou-Alfa GK, Meyer T, Cheng AL, et al. Cabozantinib in Patients with Advanced and Progressing Hepatocellular Carcinoma. *N Engl J Med*. 2018 Jul 5;379(1):54-63.
- 32e. Zhu AX, Park JO, Ryou BY, et al. Ramucirumab versus placebo as second-line treatment in patients with advanced hepatocellular carcinoma following first-line therapy with sorafenib (REACH): a randomised, double-blind, multicentre, phase 3 trial. *Lancet Oncol*. 2015 Jul;16(7):859-70.
- 33e. Zhu AX, Kang YK, Yen CJ, et al. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased α -fetoprotein concentrations (REACH-2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2019 Feb;20(2):282-296.
- 34e. Yau T, et al. Nivolumab (NIVO) + ipilimumab (IPI) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040 (abstract). *J Clin Oncol* 37, 2019 (suppl; abstr 4012). Abstract available online at <https://meetinglibrary.asco.org/record/173194/abstract> (Accessed on April 24, 2020).
- 35e. Paz-Ares L, et al. Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer. *N Engl J Med* 2018; 379:2040-2051.
- 36e. Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1–Positive Non–Small-Cell Lung Cancer. *N Engl J Med* 2016; 375:1823-1833.
- 37e. Gandhi L, et al. Pembrolizumab plus Chemotherapy in Metastatic Non–Small-Cell Lung Cancer. *N Engl J Med* 2018; 378:2078-2092.
- 38e. Planchard D, Smit EF, Groen HJM, et al. Dabrafenib plus trametinib in patients with previously untreated BRAFV600E-mutant metastatic non-small-cell lung cancer: an open-label, phase 2 trial. *Lancet Oncol*. 2017 Oct;18(10):1307-1316. doi: 10.1016/S1470-2045(17)30679-4.
- 39e. Planchard D, Kim TM, Mazieres J, et al. Dabrafenib in patients with BRAF(V600E)-positive advanced non-small-cell lung cancer: a single-arm, multicentre, open-label, phase 2 trial. *Lancet Oncol*. 2016 May;17(5):642-50. doi: 10.1016/S1470-2045(16)00077-2.
- 40e. Gautschi O, Milia J, Cabarro B, et al. Targeted Therapy for Patients with BRAF-Mutant Lung Cancer: Results from the European EURAF Cohort. *J Thorac Oncol*. 2015 Oct;10(10):1451-7. doi: 10.1097/JTO.0000000000000625.
- 41e. Drilon A, Laetsch TW, Kummar S, et al. Efficacy of Larotrectinib in TRK Fusion-Positive Cancers in Adults and Children. *N Engl J Med*. 2018;378(8):731–739. doi:10.1056/NEJMoa1714448.

- 42e. Doebele R, Paz-Ares L, Farago AF, et al. Entrectinib in NTRK-fusion positive (NTRK-FP) non-small cell lung cancer (NSCLC): Integrated analysis of patients enrolled in three trials (STARTRK-2, STARTRK-1 and ALKA-372-001)[abstract]. AACR Annual Meeting. Atlanta, GA:Abstract CT131.
- 43e. Carbone DP, Reck M, Paz-Ares L, et al. First-Line Nivolumab in Stage IV or Recurrent Non-Small-Cell Lung Cancer. *N Engl J Med.* 2017;376(25):2415–2426. doi:10.1056/NEJMoa1613493.
- 44e. West H, McCleod M, Hussein M, et al. Atezolizumab in combination with carboplatin plus nab-paclitaxel chemotherapy compared with chemotherapy alone as first-line treatment for metastatic non-squamous non-small-cell lung cancer (IMpower130): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol.* 2019;20(7):924–937. doi:10.1016/S1470-2045(19)30167-6.
- 45e. Socinski MA, Jotte RM, Cappuzzo F, et al. Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC. *N Engl J Med* 2018; 378:2288-2301. DOI: 10.1056/NEJMoa1716948.
- 46e. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet.* 2016 Apr 9;387(10027):1540-1550. doi: 10.1016/S0140-6736(15)01281-7.
- 47e. Brahmer J, Reckamp KL, Baas P, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. *N Engl J Med.* 2015;373(2):123–135. doi:10.1056/NEJMoa1504627.
- 48e. Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus Docetaxel in Advanced Nonsquamous Non-Small-Cell Lung Cancer. *N Engl J Med.* 2015;373(17):1627–1639. doi:10.1056/NEJMoa1507643.
- 49e. Barlesi F, Park K, Ciardiello F, et al. Primary analysis from OAK, a randomized phase III study comparing atezolizumab with docetaxel in 2L/3L NSCLC. *Ann of Oncol* 2016 Oct;27(suppl_6):LBA44_PR.
- 50e. Mok TS, Wu Y-L, Ahn M-J, et al. Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive Lung Cancer. *N Engl J Med.* 2017;376(7):629–640. doi:10.1056/NEJMoa1612674.
- 51e. Solomon BJ, Besse B, Bauer TM, et al. Lorlatinib in patients with ALK-positive non-small-cell lung cancer: results from a global phase 2 study [published correction appears in *Lancet Oncol.* 2019 Jan;20(1):e10]. *Lancet Oncol.* 2018;19(12):1654–1667. doi:10.1016/S1470-2045(18)30649-1.
- 52e. Ou SH, Ahn JS, De Petris L, et al. Alectinib in Crizotinib-Refractory ALK-Rearranged Non-Small-Cell Lung Cancer: A Phase II Global Study. *J Clin Oncol.* 2016;34(7):661–668. doi:10.1200/jco.2015.63.9443.
- 53e. Huber RM, Hansen KH, Paz-Ares Rodríguez L, et al. Brigatinib in Crizotinib-Refractory ALK+ NSCLC: 2-Year Follow-up on Systemic and Intracranial Outcomes in the Phase 2 ALTA Trial. *J Thorac Oncol.* 2020;15(3):404–415. doi:10.1016/j.jtho.2019.11.004.

- 54e. Shaw AT, Kim TM, Crinò L, et al. Ceritinib versus chemotherapy in patients with ALK-rearranged non-small-cell lung cancer previously given chemotherapy and crizotinib (ASCEND-5): a randomised, controlled, open-label, phase 3 trial. *Lancet Oncol*. 2017;18(7):874–886. doi:10.1016/S1470-2045(17)30339-X.
- 55e. Rini BI, Plimack ER, Stus V, et al. Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2019;380(12):1116–1127. doi:10.1056/NEJMoa1816714.
- 56e. Sternberg CN, Davis ID, Mardiak J, et al. Pazopanib in locally advanced or metastatic renal cell carcinoma: results of a randomized phase III trial. *J Clin Oncol*. 2010 Feb 20;28(6):1061-8.
- 57e. Sternberg CN, Hawkins RE, Wagstaff J, et al. A randomised, double-blind phase III study of pazopanib in patients with advanced and/or metastatic renal cell carcinoma: final overall survival results and safety update. *Eur J Cancer*. 2013 Apr;49(6):1287-96.
- 58e. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med*. 2007 Jan 11;356(2):115-24.
- 59e. Choueiri TK, Halabi S, Sanford BL, et al. Cabozantinib Versus Sunitinib As Initial Targeted Therapy for Patients With Metastatic Renal Cell Carcinoma of Poor or Intermediate Risk: The Alliance A031203 CABOSUN Trial. *J Clin Oncol*. 2016;35(6):591–597.
- 60e. Motzer RJ, Escudier B, McDermott DF, et al. Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2015;373(19):1803–1813. doi:10.1056/NEJMoa1510665.
- 61e. Hammers HJ, Plimack ER, Infante JR, et al. Safety and Efficacy of Nivolumab in Combination With Ipilimumab in Metastatic Renal Cell Carcinoma: The CheckMate 016 Study. *J Clin Oncol*. 2017;35(34):3851–3858. doi:10.1200/JCO.2016.72.1985.
- 62e. Choueiri TK, Escudier B, Powles T, et al. Cabozantinib versus Everolimus in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2015;373(19):1814–1823. doi:10.1056/NEJMoa1510016.
- 63e. Chung HC, Piha-Paul SA, Lopez-Martin J, et al. Pembrolizumab After Two or More Lines of Previous Therapy in Patients With Recurrent or Metastatic SCLC: Results From the KEYNOTE-028 and KEYNOTE-158 Studies. *J Thorac Oncol*. 2020;15(4):618–627. doi:10.1016/j.jtho.2019.12.109.
- 64e. Chung HC, Lopez-Martin JA, Kao S C-H, et al. Phase 2 study of pembrolizumab in advanced small-cell lung cancer (SCLC): KEYNOTE-158. *J Clin Oncol* 2018; 36S: ASCO# 8506.
- 65e. Ott PA, Elez E, Hirt S, et al. Pembrolizumab in Patients With Extensive-Stage Small-Cell Lung Cancer: Results From the Phase Ib KEYNOTE-028 Study. *J Clin Oncol* 2017; 35:3823.
- 66e. Reck M, Vicente D, Ciuleanu T, et al. LBA5: Efficacy and safety of nivolumab (nivo) monotherapy versus chemotherapy (chemo) in recurrent small cell lung cancer (SCLC): Results from CheckMate 331 [abstract]. *Ann Oncol* 2018;29:43.

- 67e. von Pawel J, Schiller JH, Shepherd FA, et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. *J Clin Oncol*. 1999 Feb;17(2):658-67.
- 68e. O'Brien ME, Ciuleanu TE, Tsekov H, et al. Phase III trial comparing supportive care alone with supportive care with oral topotecan in patients with relapsed small-cell lung cancer. *J Clin Oncol*. 2006 Dec 1;24(34):5441-7.
- 69e. Yamamoto N, Tsurutani J, Yoshimura N, et al. Phase II study of weekly paclitaxel for relapsed and refractory small cell lung cancer. *Anticancer Res*. 2006 Jan-Feb;26(1B):777-81.
- 70e. Smit EF, Fokkema E, Biesma B, Groen HJ, Snoek W, Postmus PE. A phase II study of paclitaxel in heavily pretreated patients with small-cell lung cancer. *Br J Cancer*. 1998;77(2):347-351. doi:10.1038/bjc.1998.54.
- 71e. Smyth JF, Smith IE, Sessa C, et al. Activity of docetaxel (Taxotere) in small cell lung cancer. The Early Clinical Trials Group of the EORTC. *Eur J Cancer*. 1994;30A(8):1058-60.
- 72e. Masuda N, Fukuoka M, Kusunoki Y, et al. CPT-11: a new derivative of camptothecin for the treatment of refractory or relapsed small-cell lung cancer. *J Clin Oncol*. 1992 Aug;10(8):1225-9.
- 73e. Pietanza MC, Kadota K, Huberman K, et al. Phase II trial of temozolomide in patients with relapsed sensitive or refractory small cell lung cancer, with assessment of methylguanine-DNA methyltransferase as a potential biomarker. *Clin Cancer Res*. 2012 Feb 15;18(4):1138-45. doi: 10.1158/1078-0432.CCR-11-2059.
- 74e. Alley EW, Lopez J, Santoro A, et al. Clinical safety and activity of pembrolizumab in patients with malignant pleural mesothelioma (KEYNOTE-028): preliminary results from a non-randomised, open-label, phase 1b trial. *Lancet Oncol*. 2017 May;18(5):623-630.
- 75e. Alley EW, Lopez J, Santoro A, et al. Long-Term Overall Survival for Patients with Malignant Pleural Mesothelioma on Pembrolizumab Enrolled in KEYNOTE-028. *J Thorac Oncol*. 2017 Jan;12(1):S294.
- 76e. Metaxas Y, Rivalland G, Mauti LA, et al. Pembrolizumab as Palliative Immunotherapy in Malignant Pleural Mesothelioma. *J Thorac Oncol*. 2018 Nov;13(11):1784-1791.
- 77e. Jassem J, Ramlau R, Santoro A, et al, "Phase III Trial of Pemetrexed Plus Best Supportive Care Compared With Best Supportive Care in Previously Treated Patients With Advanced Malignant Pleural Mesothelioma," *J Clin Oncol*, 2008, 26(10):1698-704. [PubMed 18375898]
- 78e. Zucali PA, Simonelli M, Michetti G, et al. Second-line chemotherapy in malignant pleural mesothelioma: results of a retrospective multicenter survey. *Lung Cancer*. 2012 Mar;75(3):360-7.
- 79e. Scherpereel A, Mazieres J, Greillier L, et al. Second or 3rd 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. *Ann Oncol*. 2017 Sept;28(5):mdx440.074.

- 80e. Quispel-Janssen J, van der Noort V, de Vries JF, et al. Programmed Death 1 Blockade With Nivolumab in Patients With Recurrent Malignant Pleural Mesothelioma. *J Thorac Oncol*. 2018 Oct;13(10):1569-1576.
- 81e. Popat S, Curioni-Fontecedro A, Polydoropoulou V, et al. A multicentre randomized phase III trial comparing pembrolizumab (P) versus single-agent chemotherapy (CT) for advanced pretreated malignant pleural mesothelioma (MPM): Results from the European Thoracic Oncology Platform (ETOP 9-15) PROMISE-meso trial. *Ann Oncol* 2019; 30S: ESMO #LBA91_PR.
- 82e. Kluger HM, Chiang V, Mahajan A, et al. Long-Term Survival of Patients With Melanoma With Active Brain Metastases Treated With Pembrolizumab on a Phase II Trial. *J Clin Oncol*. 2019;37(1):52–60. doi:10.1200/JCO.18.00204.
- 83e. Tawbi HA, Forsyth PA, Hodi S, et al. Efficacy and safety of the combination of nivolumab (NIVO) plus ipilimumab (IPI) in patients with symptomatic melanoma brain metastases (CheckMate 204). *J Clin Oncol* 2019; 37S.
- 84e. Goldberg SB, Gettinger SN, Mahajan A, et al. Pembrolizumab for patients with melanoma or non-small-cell lung cancer and untreated brain metastases: early analysis of a non-randomised, open-label, phase 2 trial. *Lancet Oncol*. 2016;17(7):976–983. doi:10.1016/S1470-2045(16)30053-5.
- 85e. Overman MJ, McDermott R, Leach JL, et al. Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): an open-label, multicentre, phase 2 study [published correction appears in *Lancet Oncol*. 2017 Sep;18(9):e510]. *Lancet Oncol*. 2017;18(9):1182–1191. doi:10.1016/S1470-2045(17)30422-9.
- 86e. Le DT, Uram JN, Wang H, et al. PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. *N Engl J Med*. 2015;372(26):2509–2520. doi:10.1056/NEJMoa1500596.
- 87e. Le DT, Kim TW, Van Cutsem E, et al. Phase II Open-Label Study of Pembrolizumab in Treatment-Refractory, Microsatellite Instability-High/Mismatch Repair-Deficient Metastatic Colorectal Cancer: KEYNOTE-164. *J Clin Oncol* 2020; 38:11.
- 88e. Chung HC, Ros W, Derlord JP, et al. Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study. *J Clin Oncol*. 2019;37(17):1470-1478.
- 89e. Spigel D et al. IMpower110: Interim OS Analysis of a Phase III Study of Atezolizumab (atezo) vs Platinum-Based Chemotherapy (chemo) as 1L Treatment (tx) in PD-L1–selected NSCLC [ESMO 2019 Abstract LBA78].
- 90e. Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet*. 2021 Feb 13;397(10274):592-604. doi: 10.1016/S0140-6736(21)00228-2. PMID: 33581821.
- 91e. Baas P, Scherpereel A, Nowak AK, et al. First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): a multicentre, randomised,

- open-label, phase 3 trial. *Lancet*. 2021 Jan 30;397(10272):375-386. doi: 10.1016/S0140-6736(20)32714-8. Epub 2021 Jan 21. Erratum in: *Lancet*. 2021 Feb 20;397(10275):670. PMID: 33485464.
- 92e. Lenz H-J, 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.
- 93e. Lenz H-J, Lonardi S, Zagonel V, et al. Nivolumab (NIVO) + low-dose ipilimumab (IPI) as first-line (1L) therapy in microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Two-year clinical update [abstract]. *Journal of Clinical Oncology* 2020;38:4040-4040.
- 94e. Andre T, Shiu KK, Kim TW, et al. Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 Study. *J Clin Oncol*. 2020;38(18_suppl):LBA4-LBA4.
- 95e. Motzer RJ, Penkov K, Haanen J, et al. Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2019 Mar 21;380(12):1103-1115. doi: 10.1056/NEJMoa1816047. Epub 2019 Feb 16.
- 96e. Motzer RJ, Hutson TE, Glen H, et al. Lenvatinib, everolimus, and the combination in patients with metastatic renal cell carcinoma: a randomised, phase 2, open-label, multicentre trial. *Lancet Oncol*. 2015 Nov;16(15):1473-1482. doi: 10.1016/S1470-2045(15)00290-9. Epub 2015 Oct 22. Erratum in: *Lancet Oncol*. 2016 Jul;17 (7):e270. Erratum in: *Lancet Oncol*. 2018 Oct;19(10):e509.
- 97e. Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Engl J Med*. 2021 Apr 8;384(14):1289-1300. doi: 10.1056/NEJMoa2035716.
- 98e. Yau T, Park JW, Finn RS, et al. LBA38_PR - CheckMate 459: A randomized, multi-center phase III study of nivolumab (NIVO) vs sorafenib (SOR) as first-line (1L) treatment in patients (pts) with advanced hepatocellular carcinoma (aHCC). *Ann of Oncol* 2019 Oct;30(suppl_5):v874-v875.
- 99e. Wolchok JD, Chiarion-Sileni V, Gonzalez R, et al. CheckMate 067: 6.5-year outcomes in patients (pts) with advanced melanoma. *J Clin Oncol* 2021; 39:15S.
- 100e. Pires da Silva I, Ahmed T, Reijers ILM, et al. Ipilimumab alone or ipilimumab plus anti-PD-1 therapy in patients with metastatic melanoma resistant to anti-PD-(L)1 monotherapy: a multicentre, retrospective, cohort study. *Lancet Oncol*. 2021 Jun;22(6):836-847. doi: 10.1016/S1470-2045(21)00097-8.
- 101e. Berton D, Banerjee S, Curigliano G, et al. Antitumor activity of dostarlimab in patients with mismatch repair-deficient/microsatellite instability-high tumors: A combined analysis of two cohorts in the GARNET study. *Journal of Clinical Oncology*. Volume 39, Issue 15_suppl. doi/abs/10.1200/JCO.2021.39.15_suppl.2564.

- 102e. Choueiri TK, Powles T, Burotto M, et al. 696O_PR Nivolumab + cabozantinib vs sunitinib in first-line treatment for advanced renal cell carcinoma: First results from the randomized phase III CheckMate 9ER trial. Volume 31, SUPPLEMENT 4, S1159, September 01, 2020.
- 103e. Vanderwalde AM, Moon J, Kendra K et al. S1616: Ipilimumab plus nivolumab versus ipilimumab alone in patients with metastatic or unresectable melanoma that did not respond to anti-PD-1 therapy In: Proceedings of the 113th Annual Meeting of the American Association for Cancer Research; 2021 April 8-13; New Orleans LA. Philadelphia (PA): AACR; 2022. Abstract CT013.
<https://www.abstractsonline.com/pp8/#!/10517/presentation/20155> (Accessed on June 10, 2022).
- 104e. Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and Nivolumab versus Nivolumab in Untreated Advanced Melanoma. *N Engl J Med.* 2022 Jan 6;386(1):24-34. doi: 10.1056/NEJMoa2109970.
- 105e. Kato K, Shah MA, Enzinger P, et al. KEYNOTE-590: Phase III study of first-line chemotherapy with or without pembrolizumab for advanced esophageal cancer. *Future Oncol.* 2019 Apr;15(10):1057-1066. doi: 10.2217/fo-2018-0609.
- 106e. Zalcman G, Mazieres J, Margery J, et al. Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. *Lancet.* 2016 Apr 2;387(10026):1405-1414.
- 107e. Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. *J Clin Oncol.* 2003 Jul 15;21(14):2636-44.
- 108e. Atkins MB, Lee SJ, Chmielowski B, et al. DREAMseq (Doublet, Randomized Evaluation in Advanced Melanoma Sequencing): A phase III trial—ECOG-ACRIN EA6134. *J Clin Oncol.* 2021 Dec 20;39(36_suppl):356154-356-154.
- 109e. Mok TS, Wu Y-L, Ahn M-J, et al. Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive Lung Cancer. *N Engl J Med.* 2017 Feb 16;376(7):629-640.
- 110e. André T, Lonardi S, Wong KYM, et al. Nivolumab plus low-dose ipilimumab in previously treated patients with microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer: 4-year follow-up from CheckMate 142. *Ann Oncol.* 2022 Oct;33(10):1052-1060.
- 111e. Johnson ML, Cho BC, Luft A, et al; POSEIDON investigators. Durvalumab With or Without Tremelimumab in Combination With Chemotherapy as First-Line Therapy for Metastatic Non-Small-Cell Lung Cancer: The Phase III POSEIDON Study. *J Clin Oncol.* 2022 Nov 3;JCO2200975. doi: 10.1200/JCO.22.00975.
- 112e. Gogishvili M, Melkadze T, Makharadze T, et al. LBA51 EMPOWER-Lung 3: Cemiplimab in combination with platinum doublet chemotherapy for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC). *Annals of Oncology*, ISSN: 0923-7534, Vol: 32, SUPPLEMENT 5, S1328, SEPTEMBER 01, 2021. DOI10.1016/j.annonc.2021.08.2130.

- 113e. André T, Tougeron D, Piessen G, et al. Neoadjuvant Nivolumab Plus Ipilimumab and Adjuvant Nivolumab in Localized Deficient Mismatch Repair/Microsatellite Instability-High Gastric or Esophagogastric Junction Adenocarcinoma: The GERCOR NEONIPIGA Phase II Study. *J Clin Oncol*. 2023 Jan 10;41(2):255-265.
- 114e. Ludford K, Ho WJ, Thomas JV, et al. Neoadjuvant Pembrolizumab in Localized Microsatellite Instability High/Deficient Mismatch Repair Solid Tumors. *J Clin Oncol*. 2023 Apr 20;41(12):2181-2190.
- 115e. Pietrantonio F, Raimondi A, Lonardi S, et al. INFINITY: A multicentre, single-arm, multi-cohort, phase II trial of tremelimumab and durvalumab as neoadjuvant treatment of patients with microsatellite instability-high (MSI) resectable gastric or gastroesophageal junction adenocarcinoma (GAC/GEJAC). *Journal of Clinical Oncology* 2023;41:358-358.
- 116e. Marabelle A, Fakih M, Lopez J, et al. Association of Tumor Mutational Burden with Outcomes in Patients with Select Advanced Solid Tumors Treated with Pembrolizumab in KEYNOTE-158. *Ann Oncol*. 2019;30(suppl_5):v475-v532. doi: 10.1093/annonc/mdz253.
- 117e. Novello S, Mazières J, Oh IJ, et al. Alectinib versus chemotherapy in crizotinib-pretreated anaplastic lymphoma kinase (ALK)-positive non-small-cell lung cancer: results from the phase III ALUR study. *Ann Oncol*. 2018;29(6):1409-1416. doi:10.1093/annonc/mdy121.
- 118e. Kim DW, Tiseo M, Ahn MJ, et al. Brigatinib in Patients With Crizotinib-Refractory Anaplastic Lymphoma Kinase-Positive Non-Small-Cell Lung Cancer: A Randomized, Multicenter Phase II Trial. *J Clin Oncol*. 2017 Aug 1;35(22):2490-2498. doi: 10.1200/JCO.2016.71.5904.
- 119e. Shaw AT, Kim DW, Nakagawa K, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. *N Engl J Med*. 2013 Jun 20;368(25):2385-94. doi: 10.1056/NEJMoa1214886.
- 120e. Solomon BJ, Besse B, Bauer TM, et al. Lorlatinib in patients with ALK-positive non-small-cell lung cancer: results from a global phase 2 study [published correction appears in *Lancet Oncol*. 2019 Jan;20(1):e10]. *Lancet Oncol*. 2018;19(12):1654–1667. doi:10.1016/S1470-2045(18)30649-1.
- 121e. Magellan Rx Management. Yervoy Clinical Literature Review Analysis. Last updated March 2024. Accessed March 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach

ICD-10	ICD-10 Description
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, 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
C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C23	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
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

ICD-10	ICD-10 Description
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
C40.00	Malignant neoplasm of scapula and long bones of unspecified upper limb
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.10	Malignant neoplasm of short bones of unspecified upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.20	Malignant neoplasm of long bones of unspecified lower limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.30	Malignant neoplasm of short bones of unspecified lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.80	Malignant neoplasm of overlapping sites of bone and articular cartilage of unspecified limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.90	Malignant neoplasm of unspecified bones and articular cartilage of unspecified limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb
C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified
C43.0	Malignant melanoma of lip
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

ICD-10	ICD-10 Description
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
C45.0	Mesothelioma of pleura
C46.0	Kaposi's sarcoma of skin
C46.1	Kaposi's sarcoma of soft tissue
C46.2	Kaposi's sarcoma of palate
C46.3	Kaposi's sarcoma of lymph nodes
C46.4	Kaposi's sarcoma of gastrointestinal sites
C46.50	Kaposi's sarcoma of unspecified lung
C46.51	Kaposi's sarcoma of right lung
C46.52	Kaposi's sarcoma of left lung
C46.7	Kaposi's sarcoma of other sites
C46.9	Kaposi's sarcoma, unspecified
C47.0	Malignant neoplasm of peripheral nerves of head, face and neck
C47.10	Malignant neoplasm of peripheral nerves of unspecified upper limb, including shoulder
C47.11	Malignant neoplasm of peripheral nerves of right upper limb, including shoulder
C47.12	Malignant neoplasm of peripheral nerves of left upper limb, including shoulder
C47.20	Malignant neoplasm of peripheral nerves of unspecified lower limb, including hip
C47.21	Malignant neoplasm of peripheral nerves of right lower limb, including hip
C47.22	Malignant neoplasm of peripheral nerves of left lower limb, including hip
C47.3	Malignant neoplasm of peripheral nerves of thorax

ICD-10	ICD-10 Description
C47.4	Malignant neoplasm of peripheral nerves of abdomen
C47.5	Malignant neoplasm of peripheral nerves of pelvis
C47.6	Malignant neoplasm of peripheral nerves of trunk, unspecified
C47.8	Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system
C47.9	Malignant neoplasm of peripheral nerves and autonomic nervous system, unspecified
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C4A.0	Merkel cell carcinoma of lip
C4A.10	Merkel cell carcinoma of eyelid, including canthus
C4A.111	Merkel cell carcinoma of right upper eyelid, including canthus
C4A.112	Merkel cell carcinoma of right lower eyelid, including canthus
C4A.121	Merkel cell carcinoma of left upper eyelid, including canthus
C4A.122	Merkel cell carcinoma of left lower eyelid, including canthus
C4A.20	Merkel cell carcinoma of unspecified ear and external auricular canal
C4A.21	Merkel cell carcinoma of right ear and external auricular canal
C4A.22	Merkel cell carcinoma of left ear and external auricular canal
C4A.30	Merkel cell carcinoma of unspecified part of face
C4A.31	Merkel cell carcinoma of nose
C4A.39	Merkel cell carcinoma of other parts of face
C4A.4	Merkel cell carcinoma of scalp and neck
C4A.51	Merkel cell carcinoma of anal skin
C4A.52	Merkel cell carcinoma of skin of breast

ICD-10	ICD-10 Description
C4A.59	Merkel cell carcinoma of other part of trunk
C4A.60	Merkel cell carcinoma of unspecified upper limb, including shoulder
C4A.61	Merkel cell carcinoma of right upper limb, including shoulder
C4A.62	Merkel cell carcinoma of left upper limb, including shoulder
C4A.70	Merkel cell carcinoma of unspecified lower limb, including hip
C4A.71	Merkel cell carcinoma of right lower limb, including hip
C4A.72	Merkel cell carcinoma of left lower limb, including hip
C4A.8	Merkel cell carcinoma of overlapping sites
C4A.9	Merkel cell carcinoma, 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
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
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
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
C7B.1	Secondary Merkel cell carcinoma
D37.1	Neoplasm of uncertain behavior of stomach
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ

ICD-10	ICD-10 Description
Z85.01	Personal history of malignant neoplasm of esophagus
Z85.028	Personal history of other malignant neoplasm of stomach
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.820	Personal history of malignant melanoma of skin
Z85.821	Personal history of Merkel cell carcinoma
Z85.830	Personal history of malignant neoplasm of bone
Z85.831	Personal history of malignant neoplasm of soft tissue

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied 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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC