# Opdivo® (nivolumab)
## (Intravenous)

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## I. Length of Authorization [1]

Coverage will be provided for six months and may be renewed.

- Adjuvant use in the treatment of melanoma can be authorized up to a maximum of 12 months of therapy.
- Use in the treatment of metastatic NSCLC in combination with ipilimumab for PD-L1 expressing tumors can be authorized up to a maximum of 2 years of therapy.
- Use in the treatment of metastatic or recurrent NSCLC in combination with ipilimumab and two (2) cycles of platinum-doublet chemotherapy can be authorized up to a maximum of 2 years of therapy.

## II. Dosing Limits

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

- Opdivo 40 mg/4 mL single-use vial: 2 vials per 14 days
- Opdivo 100 mg/10 mL single-use vial: 2 vials per 14 days
- Opdivo 240 mg/24 mL single-use vial: 4 vials per 14 days

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

| Indication | Billable Units (BU) | Per unit time (days) |
|---|---|---|
| Merkel Cell | 340 BU | 14 days |
| Melanoma/HCC (in combination with ipilimumab) | Initial: 140 BU | 21 days x 4 doses |
| | Followed by: 480 BU | 28 days |
| Melanoma/RCC/HCC/NSCLC (as a single agent), cHL, SCCHN, MSI-H/dMMR CRC (as a single agent), Anal Carcinoma, Gestational Trophoblastic Tumor & Urothelial Carcinoma | 480 BU | 28 days |
| Metastatic NSCLC with PD-L1 expressing tumors (in combination with ipilimumab) | 340 BU | 14 days |

| | | |
|---|---|---|
| Metastatic or recurrent NSCLC (in combination with ipilimumab and platinum-doublet chemotherapy | 380 BU | 21 days |
| SCLC (as a single agent) | 240 BU | 14 days |
| MSI-H/dMMR CRC (in combination with ipilimumab) | Initial: 340 BU | 21 days x 4 doses |
| | Followed by: 480 BU | 28 days |
| Small Bowel Adenocarcinoma, CNS Metastases from NSCLC (both as single agents) | 340 BU | 14 days |
| Small Bowel Adenocarcinoma (in combination with ipilimumab) | Initial: 340 BU | 21 days x 4 doses |
| | Followed by: 340 BU | 14 days |
| RCC (in combination with ipilimumab) | Initial: 340 BU | 21 days x 4 doses |
| | Followed by: 480 BU | 28 days |
| SCLC (in combination with ipilimumab) | Initial: 340 BU | 21 days x 4 doses |
| | Followed by: 340 BU | 14 days |
| MPM (as a single agent or in combination with ipilimumab) | 340 BU | 14 days |
| CNS Metastases from Melanoma & Uveal Melanoma (both in combination with ipilimumab) | Initial: 140 BU | 21 days x 4 doses |
| | Followed by: 340 BU | 14 days |
| CNS Metastases from Melanoma (as a single agent) | 340 BU | 14 days |
| Uveal Melanoma (as a single agent) | 1140 BU | 14 days |
| Extranodal NK/ T-Cell Lymphoma | 40 BU | 14 days |

## III. Initial Approval Criteria[1]

Coverage is provided for the following conditions:

- Patient is 18 years of age or older (unless otherwise specified); **AND**

**Universal Criteria**

- Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy (e.g., cemiplimab, avelumab, pembrolizumab, atezolizumab, durvalumab, etc.) prior to initiation of therapy, unless otherwise specified; **AND**

**Cutaneous Melanoma † Φ** [1,2,15-18]

- Patient's disease is unresectable or metastatic; **AND**
  - Used as a single agent or in combination with ipilimumab as first line therapy or as subsequent therapy after progression on prior chemotherapy; **AND**
  - Used for retreatment of disease as re-induction as a single agent or in combination with ipilimumab in patients who experienced disease control *(i.e., complete or partial response or stable disease)* from prior checkpoint inhibitor therapy, but subsequently have disease progression/relapse > 3 months after treatment discontinuation; **OR**
  - Used after maximum clinical benefit from BRAF-targeted therapy; **AND**
    - Used as a single agent or in combination with ipilimumab if checkpoint inhibitor immunotherapy was not previously used; **OR**
    - Used in combination with ipilimumab for patients who progressed on single agent checkpoint inhibitor immunotherapy; **OR**

- Used as initial therapy in combination with ipilimumab for limited resectable disease with satellite/in-transit recurrence or metastases; **OR**
- Used as adjuvant treatment as a single agent; **AND**
  - Patient has lymph node involvement and has undergone complete resection, complete lymph node dissection (CLND), therapeutic lymph node dissection (TLND), or nodal basin ultrasound surveillance; **OR**
  - Patient has satellite/in-transit metastases or recurrence and has no evidence of disease after complete excision; **OR**
  - Patient has undergone TLND and/or complete resection of nodal recurrence; **OR**
  - Patient has undergone complete resection of distant metastatic disease

**Uveal Melanoma ‡** [2,19,20]

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

**Hepatocellular Carcinoma (HCC) † Φ** [1,2,21]

- Patient locally advanced, unresectable, or metastatic disease; **AND**
- Patient has a laboratory confirmed diagnosis of hepatocellular carcinoma; **AND**
- Patient progressed on or was intolerant to sorafenib; **AND**
  - Patient has Child-Pugh Class A or B7 disease; **AND**
    - Used as a single agent; **OR**
  - Patient has Child-Pugh Class A disease; **AND**
    - Used in combination with ipilimumab

**Non-Small Cell Lung Cancer (NSCLC) †** [1,2,22,23]

- Patient has metastatic disease with a high tumor mutational burden (TMB)* (i.e., ≥10 mutations per megabase) ‡; **AND**
  - Used as a single-agent or in combination with ipilimumab as first-line therapy; **OR**
- Patient has metastatic or recurrent disease with no EGFR or ALK tumor aberrations and PS 0-1; **AND**
  - Used as first-line therapy in combination with ipilimumab and two (2) cycles of platinum-doublet chemotherapy †; **OR**
- 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 in combination with ipilimumab; **AND**
    - Used in patients with PS 0-1 who have EGFR, ALK, ROS1, BRAF, MET exon skipping mutation, and RET rearrangement negative tumors and PD-L1 expression <1% OR for BRAF V600E-mutation positive tumors or NTRK gene fusion positive tumors ‡; **OR**

        - Used in patients with PS 0-2 for PD-L1 expression-positive (≥1%) tumors that are EGFR, ALK, ROS1, BRAF, MET exon skipping mutation, and RET rearrangement negative †; **OR**
    - Used as subsequent therapy in combination with ipilimumab; **AND**
        - Used in patients with PS 0-1 who have EGFR, ALK, ROS1, BRAF, MET exon 14 skipping mutation, or RET rearrangement positive tumors and prior targeted therapy§ OR for BRAF V600E mutation positive disease or NTRK gene fusion positive tumors ‡; **OR**
    - Used as subsequent therapy as a single agent †; **AND**
        - Disease has progressed during or following cytotoxic (e.g., platinum-based) therapy

**TMB is an evolving biomarker that may be helpful in selecting patients for immunotherapy. There is no consensus on how to measure TMB.*

**Renal Cell Carcinoma (RCC) †** [1,2,25,26]

- Used in combination with ipilimumab for clear cell histology; **AND**
    - Used as first-line therapy in patients with advanced, relapsed, or stage IV disease with intermediate or poor risk; **OR**
    - Used as first-line therapy in patients with relapsed or stage IV disease with favorable risk; **OR**
    - Used as subsequent therapy in patients with relapsed or stage IV disease; **OR**
- Used as a single agent; **AND**
    - Used as subsequent therapy in patients with advanced, relapsed, or stage IV disease for clear cell histology; **OR**
    - Patient has relapsed or stage IV disease and non-clear cell histology

**Classical Hodgkin Lymphoma (cHL) † Φ** [1,2,27,28]

- Used as a single agent; **AND**
    - Patient is at least 18 years old and has received 2 or more prior lines of therapy OR used as palliative therapy in patients more than 60 years old; **AND**
        - Patient has relapsed or progressive disease after an autologous hematopoietic stem cell transplantation (HSCT) with or without brentuximab vedotin; **OR**
        - Patient has relapsed or refractory disease and is either transplant-ineligible based on comorbidities or failure of second-line chemotherapy; **OR**
        - Patient is post-allogeneic stem-cell transplant; **OR**
- Used in combination with brentuximab vedotin as second-line or subsequent therapy (if not previously used) for relapsed or refractory disease

**Squamous Cell Carcinoma of the Head and Neck (SCCHN) †** [1,2,29]

- Used as single-agent therapy; **AND**
- Patient has unresectable, recurrent, persistent, or metastatic disease; **AND**
- Disease has progressed on or after platinum-based therapy; **AND**
- Patient does not have nasopharyngeal disease

**Urothelial Carcinoma/Bladder Cancer † [1,2,30]**

- Used as a single agent; **AND**
- Used as subsequent systemic therapy after previous platinum treatment*; **AND**
- Patient has one of the following diagnoses:
  - Locally advanced or metastatic urothelial carcinoma; **OR**
  - Local bladder cancer recurrence or persistent disease in a preserved bladder ‡; **OR**
  - Local or metastatic bladder cancer recurrence post-cystectomy ‡; **OR**
  - Recurrent or metastatic primary carcinoma of the urethra ‡; **AND**
    - Patient does not have recurrence of stage T3-4 disease or palpable inguinal lymph nodes; **OR**
  - Metastatic upper genitourinary (GU) tract tumors ‡; **OR**
  - Metastatic urothelial carcinoma of the prostate ‡

***Note:***

– *If platinum treatment occurred greater than 12 months ago, the patient should be re-treated with platinum-based therapy if the patient is still platinum eligible (see below for cisplatin- or carboplatin-ineligible comorbidities).*

- *Cisplatin-ineligible comorbidities may include the following: GFR < 60 mL/min, PS ≥ 2, hearing loss of ≥ 25 decibels (dB) at two contiguous frequencies, or grades ≥ 2 peripheral neuropathy. Carboplatin may be substituted for cisplatin particularly in those patients with a GFR <60 mL/min or a PS of 2.*
- *Carboplatin-ineligible comorbidities may include the following: GFR < 30 mL/min, PS ≥ 3, grade ≥ 3 peripheral neuropathy, or NYHA class ≥ 3, etc.*

**Small Cell Lung Cancer (SCLC) † Φ [1,2,24]**

- Used as subsequent systemic therapy; **AND**
  - Used as a single agent for metastatic disease with progression after platinum-based treatment and at least one other line of therapy †; **OR**
  - Used as a single agent or in combination with ipilimumab in patients with a performance status of 0-2 ‡; **AND**
    - Used for relapse within 6 months following complete response, partial response, or stable disease with initial treatment; **AND**
      - Patient did not relapse while on maintenance atezolizumab or durvalumab; **OR**
    - Used for primary progressive disease

**Colorectal Cancer † [1,2,31,32]**

- Patient is 12 years of age or older; **AND**
- Patient's disease must be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); **AND**
- Patients must not have a diagnosis of MSI-H central nervous system metastases; **AND**
- Used as one of the following:
  - Used as subsequent therapy for advanced or metastatic disease that progressed following treatment with a fluoropyrimidine-, oxaliplatin-, and/or irinotecan-based chemotherapy; **AND**
    - Used as a single agent or in combination with ipilimumab; **OR**

- Used as primary treatment for patients after previous adjuvant FOLFOX (fluorouracil, leucovorin and oxaliplatin) or CapeOX (capecitabine-oxaliplatin) in the past 12 months ‡; **AND**
  - Used as a single agent or in combination with ipilimumab for unresectable metastatic disease; **OR**
- Used as s single agent patients who are not candidates for intensive therapy ‡; **AND**
  - Used as primary treatment for unresectable or metastatic disease; **OR**
  - Used as subsequent therapy for unresectable metastatic disease that remains unresectable after primary treatment

**Merkel Cell Carcinoma ‡** [2,4,33]

- Used as a single agent; **AND**
- Patient has disseminated metastatic disease

**Central Nervous System (CNS) Cancer ‡** [2,5,34,41,42]

- Used in one of the following treatment settings:
  - Used as initial treatment in patients with small asymptomatic brain metastases; **OR**
  - Used for relapsed disease in patients with limited brain metastases and stable systemic disease or reasonable treatment options; **OR**
  - Patient has recurrent limited brain metastases; **OR**
  - Used for recurrent disease in patients with extensive brain metastases and stable systemic disease or reasonable systemic treatment options; **AND**
- Used as a single-agent or in combination with ipilimumab for the treatment of brain metastases in patients with melanoma; **OR**
- Used as a single-agent for the treatment of brain metastases in patients with PD-L1 positive non-small cell lung cancer (NSCLC)

**Anal Carcinoma ‡** [2,6,35]

- Patient has metastatic squamous cell disease; **AND**
- Used as a single agent for subsequent therapy

**Gestational Trophoblastic Neoplasia ‡** [2,36]

- Used as single-agent therapy for multiagent chemotherapy resistant disease; **AND**
  - Patient has recurrent or progressive disease; **AND**
    - Patient has intermediate placental site trophoblastic or epithelioid trophoblastic tumor; **AND**
    - Patient was previously treated with a platinum/etoposide containing regimen; **OR**
  - Patient has methotrexate-resistant high risk disease

**Malignant Pleural Mesothelioma ‡** [2,37,38]

- Used as a single agent or in combination with ipilimumab as subsequent therapy

**Small Bowel Adenocarcinoma ‡** [2,31,39]

- Patient has advanced or metastatic disease that is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR): **AND**
- Used as single agent or in combination with ipilimumab (in one of the following settings):
  - As subsequent therapy; **OR**
  - As initial therapy in patients with prior oxaliplatin exposure in the adjuvant setting or contraindication

**Extranodal NK/ T-Cell Lymphoma ‡** [2,40]

- Used as a single agent for relapsed or refractory nasal type disease; **AND**
- Disease progressed following additional treatment with an alternative asparaginase-based chemotherapy regimen not previously used; **AND**
- Participation in a clinical trial is unavailable

† FDA Approved Indication(s); ‡ Compendia recommended indication(s); Φ Orphan Drug

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

## IV. Renewal Criteria[1,2,4-6,15-42]

Authorizations can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion reactions, complications of allogeneic hematopoietic stem cell transplantation (HSCT), severe immune-mediated adverse reactions (i.e. pneumonitis, colitis, hepatitis, endocrinopathies, nephritis/renal dysfunction, adverse skin reactions/rash, encephalitis), etc.; **AND**
- Disease response with treatment defined as stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- For the following indication(s), the patient has not exceeded a maximum of twelve (12) months of therapy:
  - Adjuvant treatment of melanoma

**Melanoma Re-induction or Subsequent therapy (metastatic or unresectable disease) ‡**

- *Refer to Section III for criteria (see Melanoma)*

## V. Dosage/Administration[1,4-6,24,31-42]

| Indication | Dose |
|---|---|
| Merkel Cell | 240 mg every 2 weeks or 3 mg/kg every 2 weeks until disease progression or unacceptable toxicity |
| Anal Cancer | 240 mg every 2 weeks, 480 mg every 4 weeks, or 3 mg/kg every 2 weeks until disease progression or unacceptable toxicity |
| Cutaneous Melanoma | Single agent (unresectable or metastatic disease):<br>• 240 mg every 2 weeks OR 480 mg every 4 weeks until disease progression or unacceptable toxicity<br>In combination with ipilimumab (unresectable or metastatic disease):<br>• 1 mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then follow with single agent regimen<br>Adjuvant treatment:<br>• 240 mg every 2 weeks or 480 mg every 4 weeks until disease recurrence or unacceptable toxicity for up to 1 year |
| Uveal Melanoma | Single agent:<br>• Up to 10 mg/kg every 2 weeks until disease progression or unacceptable toxicity<br>In combination with ipilimumab:<br>• 1 mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then 3mg/kg every 2 weeks until disease progression or unacceptable toxicity |

| | |
|---|---|
| NSCLC | Single agent:<br>• 240 mg every 2 weeks OR 480 mg every 4 weeks until disease progression or unacceptable toxicity<br>In combination with ipilimumab for metastatic disease with PD-L1 expression positive (≥1%) tumors ONLY:<br>• 3 mg/kg every 2 weeks, followed by ipilimumab 1 mg/kg every 6 weeks, until disease progression or unacceptable toxicity for up to 2 years<br>In combination with ipilimumab and platinum-doublet chemotherapy for metastatic or recurrent disease<br>• 360 mg every 3 weeks, followed by ipilimumab 1 mg/kg every 6 weeks and histology-based platinum-doublet chemotherapy every 3 weeks for 2 cycles, until disease progression or unacceptable toxicity for up to 2 years |
| cHL, SCCHN, Urothelial Carcinoma, & Gestational Trophoblastic Neoplasia (GTN) | 240 mg every 2 weeks or 480 mg every 4 weeks until disease progression or unacceptable toxicity |
| MSI-H/dMMR CRC | Adult patients and for pediatric patients ≥ 12 years and ≥ 40 kg<br>• **As a single agent:** 240 mg every 2 weeks or 480 mg every 4 weeks until disease progression or unacceptable toxicity<br>• **In combination with ipilimumab:** 3 mg/kg, followed by ipilimumab 1 mg/kg on the same day, every 3 weeks for 4 doses, then follow with the single agent regimen<br>Pediatric patients ≥ 12 years and < 40 kg<br>• **As a single agent:** 3 mg/kg every 2 weeks until disease progression or unacceptable toxicity<br>• **In combination with ipilimumab:** 3 mg/kg, followed by ipilimumab 1 mg/kg on the same day, every 3 weeks for 4 doses, then follow with the single agent regimen |
| SCLC | Single agent:<br>• 240 mg every 2 weeks until disease progression or unacceptable toxicity<br>In combination with ipilimumab:<br>• 1 mg/kg to 3 mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then 3 mg/kg every 2 weeks |
| Renal Cell Carcinoma (RCC) | Single-agent:<br>• 240 mg every 2 weeks or 480 mg every 4 weeks until disease progression or unacceptable toxicity<br>In combination with ipilimumab:<br>• 3 mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then follow with single-agent regimen |
| Hepatocellular Carcinoma (HCC) | Single-agent:<br>• 240 mg every 2 weeks or 480 mg every 4 weeks until disease progression or unacceptable toxicity<br>In combination with ipilimumab: |

| | |
|---|---|
| | • 1 mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then follow with single-agent regimen |
| Malignant Pleural Mesothelioma (MPM) | Single agent:<br>• 3 mg/kg every 2 weeks until disease progression or unacceptable toxicity<br>In combination with ipilimumab:<br>• 3 mg/kg every 2 weeks, followed by ipilimumab 1mg/kg every 6 weeks, until disease progression or unacceptable toxicity **OR**<br>• 240 mg every 2 weeks, followed by ipilimumab 1mg/kg every 6 weeks (for a total of 4 ipilimumab doses); treatment with nivolumab is continued for up to 2 years or until disease progression or unacceptable toxicity |
| CNS Metastases from Melanoma | Single agent:<br>• 3 mg/kg every 2 weeks<br>In combination with ipilimumab:<br>• 1 mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then 3 mg/kg every 2 weeks |
| CNS Metastases from NSCLC | 3 mg/kg every 2 weeks until disease progression or unacceptable toxicity |
| Small Bowel Adenocarcinoma | Single agent:<br>• 3 mg/kg every 2 weeks, or 240 mg every 2 weeks, or 480 mg every 4 weeks<br>In combination with ipilimumab:<br>• 3 mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then 3 mg/kg or 240 mg every 2 weeks |
| Extranodal NK/ T-Cell Lymphoma | 40 mg every 2 weeks |
| Dosing should be calculated using actual body weight and not flat dosing (as applicable) based on the following:<br><br>Weight ≥ 74 kg:<br>• Standard dose 240 mg IV every 2 weeks OR 480 mg IV every 4 weeks<br>Weight is 67 kg to 73 kg:<br>• Use 440 mg IV every 4 weeks<br>Weight is < 66kg:<br>• Use 400 mg IV every 4 weeks<br>*Note: This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be taken into account.* | |

## VI. Billing Code/Availability Information

HCPCS code:

- J9299 - Injection, nivolumab, 1 mg; 1 billable unit = 1 mg

NDC:

- Opdivo 40 mg/4 mL single-use vial: 00003-3772-xx
- Opdivo 100 mg/10 mL single-use vial: 00003-3774-xx
- Opdivo 240 mg/24 mL single-use vial: 00003-3734-xx

## VII. References


1. Opdivo [package insert]. Princeton, NJ; Bristol-Myers Squibb Company; May 2020. Accessed May 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) nivolumab. National Comprehensive Cancer Network, 2020. 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 May 2020.
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## Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|---|---|
| C00.0 | Malignant neoplasm of external upper lip |
| C00.1 | Malignant neoplasm of external lower lip |
| C00.2 | Malignant neoplasm of external lip, unspecified |
| C00.3 | Malignant neoplasm of upper lip, inner aspect |
| C00.4 | Malignant neoplasm of lower lip, inner aspect |
| C00.5 | Malignant neoplasm of lip, unspecified, inner aspect |
| C00.6 | Malignant neoplasm of commissure of lip, unspecified |
| C00.8 | Malignant neoplasm of overlapping sites of lip |
| C01 | Malignant neoplasm of base of tongue |
| C02.0 | Malignant neoplasm of dorsal surface of tongue |
| C02.1 | Malignant neoplasm of border of tongue |
| C02.2 | Malignant neoplasm of ventral surface of tongue |
| C02.3 | Malignant neoplasm of anterior two-thirds of tongue, part unspecified |
| C02.4 | Malignant neoplasm of lingual tonsil |
| C02.8 | Malignant neoplasm of overlapping sites of tongue |
| C02.9 | Malignant neoplasm of tongue, unspecified |
| C03.0 | Malignant neoplasm of upper gum |
| C03.1 | Malignant neoplasm of lower gum |
| C03.9 | Malignant neoplasm of gum, unspecified |
| C04.0 | Malignant neoplasm of anterior floor of mouth |
| C04.1 | Malignant neoplasm of lateral floor of mouth |
| C04.8 | Malignant neoplasm of overlapping sites of floor of mouth |
| C04.9 | Malignant neoplasm of floor of mouth, unspecified |
| C05.0 | Malignant neoplasm of hard palate |
| C05.1 | Malignant neoplasm of soft palate |

| | |
|---|---|
| C06.0 | Malignant neoplasm of cheek mucosa |
| C06.2 | Malignant neoplasm of retromolar area |
| C06.8 | Malignant neoplasm of overlapping sites of unspecified parts of mouth |
| C06.89 | Malignant neoplasm of overlapping sites of other parts of mouth |
| C06.9 | Malignant neoplasm of mouth, unspecified |
| C09.0 | Malignant neoplasm of tonsillar fossa |
| C09.1 | Malignant neoplasm of tonsillar pillar (anterior) (posterior) |
| C09.8 | Malignant neoplasm of overlapping sites of tonsil |
| C09.9 | Malignant neoplasm of tonsil, unspecified |
| C10.3 | Malignant neoplasm of posterior wall of oropharynx |
| C12 | Malignant neoplasm of pyriform sinus |
| C13.0 | Malignant neoplasm of postcricoid region |
| C13.1 | Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect |
| C13.2 | Malignant neoplasm of posterior wall of hypopharynx |
| C13.8 | Malignant neoplasm of overlapping sites of hypopharynx |
| C13.9 | Malignant neoplasm of hypopharynx, unspecified |
| C14.0 | Malignant neoplasm of pharynx, unspecified |
| C14.2 | Malignant neoplasm of Waldeyer's ring |
| C14.8 | Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx |
| C17.0 | Malignant neoplasm of duodenum |
| C17.1 | Malignant neoplasm of jejunum |
| C17.2 | Malignant neoplasm of ileum |
| C17.3 | Meckel's diverticulum, malignant |
| C17.8 | Malignant neoplasm of overlapping sites of small intestine |
| C17.9 | Malignant neoplasm of small intestine, unspecified |
| C18.0 | Malignant neoplasm of cecum |
| C18.1 | Malignant neoplasm of appendix |
| C18.2 | Malignant neoplasm of ascending colon |
| C18.3 | Malignant neoplasm of hepatic flexure |
| C18.4 | Malignant neoplasm of transverse colon |
| C18.5 | Malignant neoplasm of splenic flexure |
| C18.6 | Malignant neoplasm of descending colon |
| C18.7 | Malignant neoplasm of sigmoid colon |
| C18.8 | Malignant neoplasm of overlapping sites of colon |
| C18.9 | Malignant neoplasm of colon, unspecified |
| C19 | Malignant neoplasm of rectosigmoid junction |

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|---|---|
| C20 | Malignant neoplasm of rectum |
| C21.0 | Malignant neoplasm of anus, unspecified |
| C21.1 | Malignant neoplasm of anal canal |
| C21.2 | Malignant neoplasm of cloacogenic zone |
| C21.8 | Malignant neoplasm of overlapping sites of rectum, anus and anal canal |
| C22.0 | Liver cell carcinoma |
| C22.8 | Malignant neoplasm of liver, primary, unspecified as to type |
| C22.9 | Malignant neoplasm of liver, not specified as primary or secondary |
| C31.0 | Malignant neoplasm of maxillary sinus |
| C31.1 | Malignant neoplasm of ethmoidal sinus |
| C32.0 | Malignant neoplasm of glottis |
| C32.1 | Malignant neoplasm of supraglottis |
| C32.2 | Malignant neoplasm of subglottis |
| C32.3 | Malignant neoplasm of laryngeal cartilage |
| C32.8 | Malignant neoplasm of overlapping sites of larynx |
| C32.9 | Malignant neoplasm of larynx, 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 |
| C34.31 | Malignant neoplasm of lower lobe, right bronchus or lung |
| C34.32 | Malignant neoplasm of lower lobe, left bronchus or lung |
| C34.80 | Malignant neoplasm of overlapping sites of unspecified bronchus and lung |
| C34.81 | Malignant neoplasm of overlapping sites of right bronchus and lung |
| C34.82 | Malignant neoplasm of overlapping sites of left bronchus and lung |
| C34.90 | Malignant neoplasm of unspecified part of unspecified bronchus or lung |
| C34.91 | Malignant neoplasm of unspecified part of right bronchus or lung |
| C34.92 | Malignant neoplasm of unspecified part of left bronchus or lung |
| C38.4 | Malignant neoplasm of pleura |
| C43.0 | Malignant melanoma of lip |
| C43.10 | Malignant melanoma of unspecified eyelid, including canthus |

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| C43.111 | Malignant melanoma of right upper eyelid, including canthus |
| C43.112 | Malignant melanoma of right lower eyelid, including canthus |
| C43.121 | Malignant melanoma of left upper eyelid, including canthus |
| C43.122 | Malignant melanoma of left lower eyelid, including canthus |
| C43.20 | Malignant melanoma of unspecified ear and external auricular canal |
| C43.21 | Malignant melanoma of right ear and external auricular canal |
| C43.22 | Malignant melanoma of left ear and external auricular canal |
| 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 |
| C44.00 | Unspecified malignant neoplasm of skin of lip |
| C44.02 | Squamous cell carcinoma of skin of lip |
| C44.09 | Other specified malignant neoplasm of skin of lip |
| C45.0 | Mesothelioma of pleura |
| 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 |

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| 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 |
| 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 |
| C61 | Malignant neoplasm of prostate |
| 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 |
| C66.1 | Malignant neoplasm of right ureter |
| C66.2 | Malignant neoplasm of left ureter |
| C66.9 | Malignant neoplasm of unspecified ureter |
| C67.0 | Malignant neoplasm of trigone of bladder |
| C67.1 | Malignant neoplasm of dome of bladder |
| C67.2 | Malignant neoplasm of lateral wall of bladder |
| C67.3 | Malignant neoplasm of anterior wall of bladder |
| C67.4 | Malignant neoplasm of posterior wall of bladder |
| C67.5 | Malignant neoplasm of bladder neck |
| C67.6 | Malignant neoplasm of ureteric orifice |
| C67.7 | Malignant neoplasm of urachus |
| C67.8 | Malignant neoplasm of overlapping sites of bladder |
| C67.9 | Malignant neoplasm of bladder, unspecified |
| C68.0 | Malignant neoplasm of urethra |
| C69.30 | Malignant neoplasm of unspecified choroid |
| C69.31 | Malignant neoplasm of right choroid |
| C69.32 | Malignant neoplasm of left choroid |

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| 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 |
| C76.0 | Malignant neoplasm of head, face and neck |
| C77.0 | Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck |
| 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 |
| C78.89 | Secondary malignant neoplasm of other digestive organs |
| 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 |
| C7B.1 | Secondary Merkel cell carcinoma |
| C81.10 | Nodular sclerosis Hodgkin lymphoma, unspecified site |
| C81.11 | Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck |
| C81.12 | Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes |
| C81.13 | Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes |
| C81.14 | Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb |
| C81.15 | Nodular sclerosis Hodgkin lymphoma, lymph nodes of inguinal region and lower limb |
| C81.16 | Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes |
| C81.17 | Nodular sclerosis Hodgkin lymphoma, spleen |
| C81.18 | Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites |
| C81.19 | Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites |
| C81.20 | Mixed cellularity Hodgkin lymphoma, unspecified site |
| C81.21 | Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck |
| C81.22 | Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes |
| C81.23 | Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes |
| C81.24 | Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb |
| C81.25 | Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb |
| C81.26 | Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes |

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| C81.27 | Mixed cellularity Hodgkin lymphoma, spleen |
| C81.28 | Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites |
| C81.29 | Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites |
| C81.30 | Lymphocyte depleted Hodgkin lymphoma, unspecified site |
| C81.31 | Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck |
| C81.32 | Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes |
| C81.33 | Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes |
| C81.34 | Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb |
| C81.35 | Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb |
| C81.36 | Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes |
| C81.37 | Lymphocyte depleted Hodgkin lymphoma, spleen |
| C81.38 | Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites |
| C81.39 | Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites |
| C81.40 | Lymphocyte-rich Hodgkin lymphoma, unspecified site |
| C81.41 | Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck |
| C81.42 | Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes |
| C81.43 | Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes |
| C81.44 | Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb |
| C81.45 | Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb |
| C81.46 | Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes |
| C81.47 | Lymphocyte-rich Hodgkin lymphoma, spleen |
| C81.48 | Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites |
| C81.49 | Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites |
| C81.70 | Other Hodgkin lymphoma unspecified site |
| C81.71 | Other Hodgkin lymphoma lymph nodes of head, face, and neck |
| C81.72 | Other Hodgkin lymphoma intrathoracic lymph nodes |
| C81.73 | Other Hodgkin lymphoma intra-abdominal lymph nodes |
| C81.74 | Other Hodgkin lymphoma lymph nodes of axilla and upper limb |
| C81.75 | Other Hodgkin lymphoma lymph nodes of inguinal region and lower limb |
| C81.76 | Other Hodgkin lymphoma intrapelvic lymph nodes |
| C81.77 | Other Hodgkin lymphoma spleen |
| C81.78 | Other Hodgkin lymphoma lymph nodes of multiple sites |
| C81.79 | Other Hodgkin lymphoma extranodal and solid organ sites |
| C81.90 | Hodgkin lymphoma, unspecified site |
| C81.91 | Hodgkin lymphoma, unspecified lymph nodes of head, face, and neck |
| C81.92 | Hodgkin lymphoma, unspecified intrathoracic lymph nodes |

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| C81.93 | Hodgkin lymphoma, unspecified intra-abdominal lymph nodes |
| C81.94 | Hodgkin lymphoma, unspecified lymph nodes of axilla and upper limb |
| C81.95 | Hodgkin lymphoma, unspecified lymph nodes of inguinal region and lower limb |
| C81.96 | Hodgkin lymphoma, unspecified intrapelvic lymph nodes |
| C81.97 | Hodgkin lymphoma, unspecified spleen |
| C81.98 | Hodgkin lymphoma, unspecified lymph nodes of multiple sites |
| C81.99 | Hodgkin lymphoma, unspecified extranodal and solid organ sites |
| C84.90 | Mature T/NK-cell lymphomas, unspecified, unspecified site |
| C84.91 | Mature T/NK-cell lymphomas, unspecified, lymph nodes of head, face, and neck |
| C84.92 | Mature T/NK-cell lymphomas, unspecified, intrathoracic lymph nodes |
| C84.93 | Mature T/NK-cell lymphomas, unspecified, intra-abdominal lymph nodes |
| C84.94 | Mature T/NK-cell lymphomas, unspecified, lymph nodes of axilla and upper limb |
| C84.95 | Mature T/NK-cell lymphomas, unspecified, lymph nodes of inguinal region and lower limb |
| C84.96 | Mature T/NK-cell lymphomas, unspecified, intrapelvic lymph nodes |
| C84.97 | Mature T/NK-cell lymphomas, unspecified, spleen |
| C84.98 | Mature T/NK-cell lymphomas, unspecified, lymph nodes of multiple sites |
| C84.99 | Mature T/NK-cell lymphomas, unspecified, extranodal and solid organ sites |
| C84.Z0 | Other mature T/NK-cell lymphomas, unspecified site |
| C84.Z1 | Other mature T/NK-cell lymphomas, lymph nodes of head, face, and neck |
| C84.Z2 | Other mature T/NK-cell lymphomas, intrathoracic lymph nodes |
| C84.Z3 | Other mature T/NK-cell lymphomas, intra-abdominal lymph nodes |
| C84.Z4 | Other mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb |
| C84.Z5 | Other mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb |
| C84.Z6 | Other mature T/NK-cell lymphomas, intrapelvic lymph nodes |
| C84.Z7 | Other mature T/NK-cell lymphomas, spleen |
| C84.Z8 | Other mature T/NK-cell lymphomas, lymph nodes of multiple sites |
| C84.Z9 | Other mature T/NK-cell lymphomas, extranodal and solid organ sites |
| C86.0 | Extranodal NK/T-cell lymphoma, nasal type |
| D09.0 | Carcinoma in situ of bladder |
| D37.01 | Neoplasm of uncertain behavior of lip |
| D37.02 | Neoplasm of uncertain behavior of tongue |
| D37.05 | Neoplasm of uncertain behavior of pharynx |
| D37.09 | Neoplasm of uncertain behavior of other specified sites of the oral cavity |
| D38.0 | Neoplasm of uncertain behavior of larynx |
| D38.5 | Neoplasm of uncertain behavior of other respiratory organs |
| D38.6 | Neoplasm of uncertain behavior of respiratory organ, unspecified |

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| D39.2 | Neoplasm of uncertain behavior of placenta |
| D39.8 | Neoplasm of uncertain behavior of other specified female genital organs |
| D39.9 | Neoplasm of uncertain behavior of female genital organ, 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 |
| Z85.21 | Personal history of malignant neoplasm of larynx |
| Z85.22 | Personal history of malignant neoplasm of nasal cavities, middle ear, and accessory sinuses |
| Z85.51 | Personal history of malignant neoplasm of bladder |
| Z85.528 | Personal history of other malignant neoplasm of kidney |
| Z85.59 | Personal history of malignant neoplasm of other urinary tract organ |
| Z85.71 | Personal history of Hodgkin lymphoma |
| Z85.810 | Personal history of malignant neoplasm of tongue |
| Z85.818 | Personal history of malignant neoplasm of other sites of lip, oral cavity and pharynx |
| Z85.819 | Personal history of malignant neoplasm of unspecified site of lip, oral cavity and pharynx |
| Z85.820 | Personal history of malignant melanoma of skin |
| Z85.821 | Personal history of Merkel cell carcinoma |

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

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

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

| **Jurisdiction(s):** 6, K | **NCD/LCD/Article Document (s):** A54862 |
|---|---|
| https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A54862&bc=gAAAAAAAAAAAAA== | |

| **Jurisdiction(s):** 15 | **NCD/LCD/Article Document (s):** A57315 |
|---|---|
| https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A57315&bc=gAAAAAAAAAAAAA | |

| **Jurisdiction(s):** J&M | **NCD/LCD/Article Document (s):** A56141 |
|---|---|
| https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56141&bc=gAAAAAAAAAAA | |

| 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 |