Opdivo® (nivolumab)
(Intravenous)

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I. Length of Authorization Δ 1,43,47,49,50,52-54,65,68,72,73,79,81,82,89,129,130

- Initial: Prior authorization validity will be provided initially for 6 months, unless otherwise specified.
  - Use in the treatment of Classical Hodgkin Lymphoma (cHL):
    - ❖ Adult cHL in combination with brentuximab vedotin: Prior authorization validity may be provided up to a maximum of 24 weeks of therapy (8 doses).
    - ❖ Pediatric cHL in combination with brentuximab vedotin-based therapy: Prior authorization validity may be provided up to a maximum of 12 weeks of therapy (4 doses).
    - ❖ Adult and Pediatric cHL in combination with ICE (ifosfamide, carboplatin, etoposide): Prior authorization validity may be provided up to a maximum of 12 weeks of therapy (6 doses).
    - ❖ Adult and Pediatric cHL in combination with AVD (doxorubicin, vinblastine, dacarbazine): Prior authorization validity may be provided up to a maximum of 24 weeks of therapy (12 doses).
  - Use in the treatment of Cutaneous Melanoma:
    - ❖ Cutaneous Melanoma neoadjuvant therapy in combination with ipilimumab: Prior authorization validity may be provided for a maximum of 2 doses.
    - ❖ Cutaneous Melanoma adjuvant treatment in combination with ipilimumab: Prior authorization validity may be provided for a maximum of 4 doses.
  - Merkel Cell Carcinoma neoadjuvant therapy: Prior authorization validity may be provided for up to a maximum of 2 doses.
- Renewal: Prior authorization validity may be renewed every 6 months thereafter, unless otherwise specified.

- Esophageal and Esophagogastric/Gastroesophageal Junction Cancer neoadjuvant or perioperative therapy: Prior authorization validity may be provided for a maximum of 12 weeks of pre-operative therapy (6 doses), followed by a maximum of 36 weeks (9 doses) of postoperative therapy after surgery.
- Gastric Cancer neoadjuvant or perioperative therapy: Prior authorization validity may be provided for a maximum of 12 weeks of pre-operative therapy (6 doses), followed by a maximum of 36 weeks (9 doses) of postoperative therapy after surgery.
- Non-Small Cell Lung Cancer neoadjuvant treatment followed by optional adjuvant treatment: Prior authorization validity may be provided for a maximum of 4 neoadjuvant doses and 13 adjuvant doses.
- Prior authorization validity may NOT be renewed for the following indications:
  - Adult cHL in combination with brentuximab vedotin
  - Pediatric cHL in combination with brentuximab vedotin-based therapy
  - Adult and Pediatric cHL in combination with ICE (ifosfamide, carboplatin, etoposide)
  - Adult and Pediatric cHL in combination with AVD (doxorubicin, vinblastine, dacarbazine)
  - Merkel Cell Carcinoma (neoadjuvant therapy)
  - Cutaneous Melanoma (neoadjuvant therapy)
  - Cutaneous Melanoma (adjuvant therapy in combination with ipilimumab)
- Prior authorization validity may be renewed up to a maximum of 1 year of therapy* for the following:
  - Cutaneous Melanoma (adjuvant therapy single agent)
  - Esophageal and Esophagogastric/Gastroesophageal Junction Cancer (adjuvant therapy following neoadjuvant chemoradiotherapy)
  - Squamous Cell Skin Cancer (weight-based 3mg/kg dosing)
  - Urothelial Carcinoma (adjuvant therapy)
- Prior authorization validity may be renewed up to a maximum of 2 years of therapy* for the following:
  - Biliary Tract Cancer (subsequent therapy)
  - Bone Cancer
  - Cervical Cancer
  - Esophageal and Esophagogastric/Gastroesophageal Junction Cancer [first-line therapy, subsequent therapy (excluding single agent use for squamous cell carcinoma)]
  - Gastric Cancer (first-line therapy)
  - Kaposi Sarcoma (in combination with ipilimumab)

- ❖ Renal Cell Carcinoma (in combination with cabozantinib)
- ❖ Pleural Mesothelioma (first-line/induction therapy in combination with ipilimumab)**
- ❖ Peritoneal Mesothelioma (first-line therapy in combination with ipilimumab)**
- ❖ Non-Small Cell Lung Cancer (in combination with ipilimumab with or without platinum-doublet chemotherapy)
- ❖ Squamous Cell Skin Cancer (flat 240 mg dosing)
- ❖ Vaginal Cancer
- ❖ Vulvar Cancer
- ❖ Urothelial Carcinoma (first line therapy in combination with gemcitabine and cisplatin, followed by single-agent maintenance therapy)

*** Including pericardial mesothelioma and tunica vaginalis testis mesothelioma*

Note: The maximum number of doses is dependent on the dosing frequency and duration of therapy. Refer to Section V for exact dosage.		
Dosing Frequency	**Maximum length of therapy**	**Maximum number of doses**
2 weeks	1 year	26 doses
	2 years	52 doses
3 weeks	2 years	35 doses
4 weeks	1 year	13 doses
	2 years	26 doses

II. Dosing Limits

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

Indication	Billable Units (BU)	Per unit time (days)
Biliary, Bone, cHL, Cutaneous Melanoma, Gastric, Gestational Trophoblastic Neoplasia (GTN), SCCHN, HCC, Kaposi Sarcoma, RCC, Soft Tissue Sarcoma, Vulvar Cancer, Vaginal Cancer & Cervical Cancer	1440 billable units	84 days
Anal, Appendiceal, CLL/SLL, CNS cancers, CRC, Esophageal and Esophagogastric/Gastroesophageal Junction Cancer, Merkel Cell, PM, PeM, Pericardial Mesothelioma, Tunica Vaginalis Testis Mesothelioma, Squamous Cell Skin, PMBCL, NSCLC, SCLC, Small Bowel Adenocarcinoma	2040 billable units	84 days
Uveal Melanoma	6960 billable units	84 days
Ampullary Adenocarcinoma	*Initial* 340 billable units	21 days x 4 doses
	Maintenance 680 billable units	28 days

Urothelial Carcinoma (Bladder Cancer)	*Initial* 360 billable units	21 days x 6 doses
	Maintenance 480 billable units	28 days

III. Initial Approval Criteria [1]

Prior authorization validity is provided for the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **AND**

Universal Criteria

- Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy, unless otherwise specified [Δ]; **AND**
- Therapy will not be used concomitantly with subcutaneous nivolumab; **AND**

Ampullary Adenocarcinoma ‡ [2,194e]

- 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 in combination with ipilimumab; **AND**
- Patient has intestinal type disease; **AND**
  - Used as first-line therapy for metastatic disease; **OR**
  - Used as subsequent therapy; **AND**
    - Patient progressed on or was intolerant to a prior line of treatment that included a fluoropyrimidine AND oxaliplatin or irinotecan, unless contraindicated

Anal Carcinoma ‡ [2,6,35]

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

Biliary Tract Cancers (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma) ‡ [2,72,177e]

- 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 in combination with ipilimumab; **AND**
  - Used as subsequent treatment for progression on or after systemic treatment for unresectable, gross residual (R2), or metastatic disease; **AND**

- Disease is refractory to standard therapies or there are no standard treatment options available; **AND**

> ➢ Use of nivolumab will be restricted to patients with a contraindication or intolerance to pembrolizumab

Urothelial Carcinoma (Bladder Cancer) † ‡ [1,2,30,51,62,92]

- Used as a single agent; **AND**
  - Used for locally advanced or metastatic urothelial carcinoma that progressed during or following platinum-containing chemotherapy* †; **OR**
  - Used as adjuvant therapy; **AND**
    - Patient has urothelial carcinoma of the bladder †, male bulbar urethra, prostate with stromal invasion, or upper genitourinary (GU) tract (ureter or renal pelvis) †; **AND**
    - Patient is at high risk for disease recurrence**; **OR**
- Used in combination with cisplatin and gemcitabine followed by nivolumab maintenance therapy; **AND**
  - Used as first-line systemic therapy in cisplatin eligible patients*; **AND**
  - Patient has one of the following diagnoses:
    - Locally advanced, unresectable, or metastatic urothelial carcinoma
    - Muscle invasive bladder cancer with local recurrence or persistent disease in a preserved bladder
    - Metastatic or local bladder cancer recurrence post-cystectomy
    - Primary carcinoma of the urethra; **AND**
      - Clinical stage T3-4, cN1-2 disease or cN1-2 palpable inguinal lymph nodes; **OR**
      - Recurrent or metastatic disease (excluding recurrence of stage T3-4 disease or palpable inguinal lymph nodes)
    - Metastatic upper genitourinary (GU) tract tumors
    - Metastatic urothelial carcinoma of the prostate

Note: [10,51,60,70]

- *If patient was progression free for >12 months after platinum therapy, consider re-treatment with platinum-based therapy if the patient is still platinum eligible (see below for cisplatin- or platinum-ineligible comorbidities).*
  - *Cisplatin-ineligible comorbidities may include the following: CrCl < 60 mL/min, ECOG PS ≥ 2 or KPS ≤ 70%, hearing loss of ≥ 25 decibels (dB) at two contiguous frequencies, grade ≥ 2 peripheral*

neuropathy, or NYHA Heart Failure class ≥ 3. Carboplatin may be substituted for cisplatin in the metastatic setting for cisplatin-ineligible patients such as those with a GFR less than 60 mL/min.

- *Platinum-ineligible comorbidities may include the following: CrCl < 30 mL/min, ECOG PS ≥ 3, grade ≥ 2 peripheral neuropathy, or NYHA Heart Failure class > 3, etc.*

***** Note:*** [1,62]

- *High risk for disease recurrence is defined as:*
  - *ypT2-ypT4a or ypN+ for patients who received neoadjuvant platinum-based therapy (excluding urothelial carcinoma of the prostate with stromal invasion);* ***OR***
  - *pT3-pT4a or pN+ for patients who did not receive neoadjuvant platinum-based therapy*

Bone Cancers ‡ [2,72,176e]

- Patient has one of the following: Ewing Sarcoma*, Chondrosarcoma, Osteosarcoma, or Chordoma; **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**
- Used in combination with ipilimumab; **AND**
- Patient has unresectable or metastatic disease that progressed following prior treatment; **AND**
- Patient has no satisfactory alternative treatment options; **AND**

- Use of nivolumab will be restricted to patients with a contraindication or intolerance to pembrolizumab

**Other primary round cell tumors of the bone (eg, CIC::DUX4, BCOR::CCNB3) can be treated like Ewing Sarcoma*

Adult Central Nervous System (CNS) Cancers ‡ [2,5,34,41,42]

- Used in one of the following treatment settings:
  - Used as initial treatment in patients with small asymptomatic limited brain metastases for newly diagnosed or stable systemic disease or if reasonable systemic treatment options exist
  - Used for recurrent limited brain metastases
  - Used as primary treatment in patients with small asymptomatic extensive brain metastases
  - Used for recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options; **AND**
  - Used in combination with ipilimumab for the treatment of brain metastases in patients with BRAF non-specific melanoma

Pediatric Central Nervous System (CNS) Cancers ‡ [2,71,274e]

- Patient is ≤ 21 years of age; **AND**
- Patient has hypermutant diffuse high-grade glioma; **AND**
  - Used for recurrent or progressive disease as a single agent *(excluding oligodendroglioma, IDH-mutant and 1p/19q co-deleted or astrocytoma IDH-mutant)*; **OR**
  - Used as adjuvant therapy *(excluding diffuse midline glioma, H3 K27-altered or pontine location)*; **AND**
    - Patient is < 3 years of age and used as a single agent; **OR**
    - Patient is ≥ 3 years of age and used following standard brain radiation therapy (RT) with or without concurrent temozolomide

Cervical Cancer ‡ [2,49,63]

- Used as subsequent therapy as a single agent; **AND**
- Patient has recurrent or metastatic disease; **AND**
- Tumor expresses PD-L1 (e.g., CPS ≥1) as determined by an FDA-approved or CLIA-compliant test❖

Colorectal Cancer (CRC) † ‡ [1,2,31,32,59,106e,107e,197e]

- Patient is at least 12 years of age; **AND**
  - Patient has microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
    - Used in combination with ipilimumab or as a single agent; **AND**
      - Used as primary/initial treatment for unresectable or medically inoperable, recurrent, advanced, or metastatic disease; **OR**
      - Used as subsequent therapy for unresectable or medically inoperable, advanced, or metastatic disease; **AND**
        - Disease progressed following treatment with a fluoropyrimidine-, oxaliplatin-, and/or irinotecan-based chemotherapy, unless contraindicated; **OR**
    - Used in combination with ipilimumab; **AND**
      - Used as neoadjuvant therapy for advanced or metastatic disease; **OR**
  - Patient has polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype [e.g., tumor mutational burden (TMB) >50 mut/Mb] as determined by an FDA-approved or CLIA-compliant test❖; **AND**
    - Used as a single agent; **AND**

- Used as subsequent therapy for locally unresectable or medically inoperable disease, advanced, or metastatic disease

Appendiceal Adenocarcinoma – Colon Cancer ‡ [2,31,59]

- Patient has microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Used in combination with ipilimumab or as a single agent; **AND**
    - Patient has advanced or metastatic disease; **AND**
      - Used as primary or initial treatment; **OR**
      - Used as subsequent treatment; **AND**
        - Disease progressed following treatment with a fluoropyrimidine-, oxaliplatin-, and/or irinotecan-based chemotherapy, unless contraindicated; **OR**
- Patient has polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype [e.g., tumor mutational burden (TMB) >50 mut/Mb] as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Used as a single agent; **AND**
  - Patient has advanced or metastatic disease

Esophageal Cancer and Esophagogastric/Gastroesophageal Junction Cancers † ‡ Φ [1,2,44,52,56,69,133e,158e]

- Used as first-line therapy; **AND**
  - Patient has squamous cell carcinoma; **AND**
    - Patient is not a surgical candidate or has unresectable advanced, recurrent, or metastatic disease; **AND**
      - Used in combination with ipilimumab OR in combination with fluorouracil or capecitabine AND cisplatin or oxaliplatin; **AND**
        - Tumor expresses PD-L1 (CPS ≥1) as determined by an FDA-approved or CLIA compliant test❖; **AND**

Used in combination with ipilimumab ONLY:

- Use of nivolumab will be restricted to patients with a contraindication or intolerance to one of the following:
  - Nivolumab/(fluorouracil or capecitabine)/(cisplatin or oxaliplatin)
  - Pembrolizumab/(fluorouracil or capecitabine)/(cisplatin or oxaliplatin); **OR**

- Patient has adenocarcinoma; **AND**
  - Patient is not a surgical candidate or has unresectable advanced, recurrent, or metastatic disease; **AND**
  - Used in combination with oxaliplatin and either fluorouracil or capecitabine for HER2 negative disease; **AND**
  - Tumor expresses PD-L1 (CPS ≥1) as determined by an FDA-approved or CLIA compliant test❖; **OR**
- Used as subsequent therapy; **AND**
  - Patient has squamous cell carcinoma †; **AND**
  - Patient is not a surgical candidate or has unresectable advanced, recurrent, or metastatic disease; **AND**
  - Used as a single agent; **AND**
  - Patient is refractory or intolerant to at least one prior fluoropyrimidine- and platinum-based regimen; **OR**
- Used as adjuvant/postoperative treatment of completely resected disease; **AND**
  - Patient has squamous cell carcinoma or adenocarcinoma; **AND**
  - Used as a single agent in patients with residual disease following neoadjuvant/preoperative chemoradiotherapy (CRT); **OR**
- Used as neoadjuvant or perioperative therapy; **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**
  - Patient has adenocarcinoma; **AND**
    - Used in combination with ipilimumab; **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; **OR**
    - Used as a single agent; **AND**
      - Used as postoperative management following R0 resection in patients who have received preoperative therapy with nivolumab and ipilimumab

Gastric Cancer † ‡ Φ [1,2,53,56]

- Used as first-line therapy; **AND**
  - Patient is not a surgical candidate or has unresectable, advanced, recurrent, or metastatic disease; **AND**

        - Used in combination with oxaliplatin and either fluorouracil or capecitabine for HER2 negative disease; **AND**
            - Tumor expresses PD-L1 (CPS ≥1) as determined by an FDA-approved or CLIA compliant test❖; **OR**
            - Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖ (independent of PD-L1 status); **OR**
- Used as neoadjuvant or perioperative therapy; **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 in combination with ipilimumab; **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; **OR**
        - Used as a single agent; **AND**
            - Used as postoperative management following R0 resection in patients who have received preoperative therapy with nivolumab and ipilimumab

Gestational Trophoblastic Neoplasia ‡ [2,36, 203e,230e]

- Used in combination with ipilimumab; **AND**
- Patient has multiagent chemotherapy-resistant disease; **AND**
    - Patient has intermediate placental site trophoblastic tumor (PSTT) or epithelioid trophoblastic tumor (ETT); **AND**
        - Patient has recurrent or progressive disease; **OR**
    - Patient has high risk disease (i.e., ≥7 Prognostic score or stage IV disease); **AND**

- Use of nivolumab will be restricted to patients with a contraindication or intolerance to avelumab

Squamous Cell Carcinoma of the Head and Neck (SCCHN) † ‡ [1,2,29,78]

- Patient has Very Advanced Head and Neck Cancer*; **AND**
- Patient has NON-nasopharyngeal cancer; **AND**
    - Used as a single agent; **AND**
        - Patient has unresectable, recurrent, persistent, or metastatic disease; **AND**
        - Disease has progressed on or after platinum-containing chemotherapy; **OR**
    - Used in combination with cetuximab for patients with performance status (PS) 0-1; **AND**

- Used as subsequent therapy for platinum-resistant or platinum-ineligible disease; **OR**
- Used as first-line therapy for one of the following:
  - Metastatic disease at initial presentation
  - Recurrent/persistent disease with distant metastases
  - Unresectable locoregional recurrence with prior RT
  - Unresectable second primary with prior RT
  - Unresectable persistent disease with prior RT; **AND**

- Use of nivolumab will be restricted to patients with a contraindication or intolerance to one of the following regimens:
  - Pembrolizumab/(cisplatin or carboplatin)/5-FU
  - Generically available agent/regimen (e.g., cisplatin/paclitaxel, etc. *[see NCCN Head and Neck Cancers guideline for complete list of alternatives]*)

** Very Advanced Head and Neck Cancer includes: newly diagnosed (M0) locally advanced T4b, N0-3 disease, newly diagnosed unresectable regional nodal disease, or those unfit for surgery, metastatic disease at initial presentation (M1), or recurrent or persistent disease with or without distant metastases.*

Hepatocellular Carcinoma (HCC) † ‡ Φ [1,2,21,86,87,38e-40e]

- Patient does not have Child-Turcotte-Pugh (CTP) Class C liver disease; **AND**
  - Used as first-line therapy; **AND**
    - Used in combination with ipilimumab; **AND**
    - Used for one of the following:
      - Unresectable disease
      - Extrahepatic/metastatic disease and is deemed ineligible for resection, transplant, or locoregional therapy; **AND**

    - Use of nivolumab will be restricted to patients with a contraindication or intolerance to tremelimumab/durvalumab; **OR**

  - Used as subsequent therapy; **AND**
    - Used in combination with ipilimumab; **AND**
    - Used for one of the following:
      - Patient was previously treated with sorafenib **†**
      - Patient had disease progression on or after systemic therapy and has not previously been treated with anti-CTLA4-based combinations

Adult Classical Hodgkin Lymphoma (cHL) † ‡ Φ [1,2,27,28,54,73,117-118,75e]

- Used as a single agent; **AND**
  - Patient has relapsed or progressive disease after autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin **†**; **OR**
  - Used for disease that is refractory to at least 3 prior lines of therapy that includes autologous HSCT **†**; **OR**
  - Used post-allogeneic hematopoietic cell transplant; **OR**
- Used in combination with ICE (ifosfamide, carboplatin, etoposide); **AND**
  - Used as subsequent therapy for suspected relapse or primary refractory disease; **OR**
- Used in combination with brentuximab vedotin; **AND**
  - Used as subsequent therapy for suspected relapse or primary refractory disease; **OR**
  - Used as primary treatment for patients who are not candidates for anthracycline therapy; **AND**
    - Used in combination with ISRT; **AND**
    - Use of nivolumab will be restricted to patients with a contraindication or intolerance to brentuximab vedotin in combination with dacarbazine; **OR**
- Used in combination with doxorubicin, vinblastine, and dacarbazine (AVD); **AND**
  - Used as primary treatment for stage III-IV disease

Pediatric Classical Hodgkin Lymphoma (cHL) ‡ [2,27,28,55,117-118,131-132]

- Patient is ≤ 18 years of age* unless otherwise specified; **AND**
  - Used as primary treatment for stage III-IV disease; **AND**
    - Used in combination with doxorubicin, vinblastine and dacarbazine (AVD) *(applies to patients ≥12 years of age ONLY)*; **OR**
  - Patient has relapsed or refractory disease; **AND**
    - Used in combination with ifosfamide, carboplatin, etoposide (ICE)**; **OR**
    - Used as a single agent**; **AND**
      - Patient is heavily pretreated with platinum or anthracycline-based chemotherapy or a decrease in cardiac function was observed; **OR**
    - Used in combination with brentuximab vedotin with or without bendamustine; **AND**
      - Patient is heavily pretreated with platinum or anthracycline-based chemotherapy or a decrease in cardiac function was observed; **AND**

- Used as re-induction therapy or as subsequent therapy (if not previously used); **OR**
- Used as re-induction therapy in highly favorable patients who may avoid autologous stem cell rescue (ASCR) (i.e., initial stage other than IIIB or IVB, no prior exposure to RT, duration of CR1 >1 year, absence of extranodal disease or B symptoms at relapse); **AND**
  - ♦ Used in combination with involved-site radiation therapy (ISRT)

** Pediatric Classic Hodgkin Lymphoma may be applicable to adolescent and young adult (AYA) patients up to the age of 39 years*

*.**There is no pediatric data for this regimen*

Kaposi Sarcoma ‡ [2,79,231e]

- Used in combination with ipilimumab; **AND**
- Used as subsequent therapy; **AND**
- Used for relapsed/refractory advanced T1, extensive T0 cutaneous, or nodal disease; **AND**
- Disease has progressed on or not responded to first-line therapy; **AND**
- Disease has progressed on alternate first-line therapy

Renal Cell Carcinoma (RCC) † ‡ [1,2,25,26,66e,164e,206e]

- Used in combination with ipilimumab; **AND**
  - Patient has clear cell histology; **AND**
  - Used as first-line therapy; **AND**
    - Patient has poor or intermediate risk advanced disease **†**; **OR**
    - Patient has 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 and clear cell histology; **OR**
- Used in combination with cabozantinib (Cabometyx only); **AND**
  - Patient has clear cell histology; **AND**
    - Used as first-line therapy for advanced, relapsed, or stage IV disease*; **AND**
    - Use of nivolumab will be restricted to patients with a contraindication or intolerance to pembrolizumab/lenvatinib; **OR**
  - Patient has non-clear cell histology; **AND**
    - Patient has relapsed or stage IV disease*; **AND**

- Patient does not have chromophobe RCC

**When used as first-line therapy for stage IV disease, disease must be M1 or unresectable T4, M0*

Cutaneous Melanoma † ‡ Φ [1,2,15-18,82,93,14e,150e-152e]

- 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 ipilimumab; **OR**
- Used as subsequent therapy for unresectable or metastatic* disease; **AND**
  - Patient is at least 12 years of age; **AND**
  - Used after disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy; **AND**
  - Used as a single agent or in combination with ipilimumab; **OR**
- Used as adjuvant treatment; **AND**
  - Used as a single agent; **AND**
    - Patient is at least 12 years of age; **AND**
      - Patient has stage IIB, stage IIC, or metastatic disease and has undergone complete resection †; **OR**
      - Patient has stage III disease; **AND**
        - Patient has undergone complete resection †; **OR**
        - Patient has resected sentinel node positive disease, during radiographic surveillance OR after complete lymph node dissection (CLND); **OR**
        - Patient has clinically positive node(s) following wide excision of the primary tumor and therapeutic lymph node dissection (TLND); **OR**
        - Patient has clinical satellite/in-transit metastases and has no evidence of disease (NED) after complete excision to clear margins; **OR**
        - Used following wide excision alone or wide excision with negative sentinel lymph node biopsy *(stage IIIB/C/D disease only)*; **OR**
        - Used for disease that is sentinel lymph node negative or sentinel lymph node biopsy not performed *(stage IIIB/C/D disease only)*; **OR**
      - Patient has local satellite/in-transit recurrence and has NED after complete excision; **OR**
      - Patient has resectable disease limited to nodal recurrence following excision and complete TLND; **OR**

        - Patient has oligometastatic disease and no evidence of disease (NED) following metastasis-directed therapy (i.e., T-VEC/intralesional therapy, stereotactic ablative therapy or complete resection) or systemic therapy followed by resection; **OR**
    - Used in combination with ipilimumab; **AND**
        - Patient has oligometastatic disease and no evidence of disease following metastasis-directed therapy (i.e., complete resection, stereotactic ablative therapy or T-VEC/intralesional therapy) or systemic therapy followed by resection; **OR**
- Used as neoadjuvant therapy; **AND**
    - Used in combination with ipilimumab; **AND**
        - Patient has stage III disease; **AND**
            - Used as primary treatment for clinically positive, resectable nodal disease; **OR**
            - Used for limited resectable disease with clinical satellite/in-transit metastases; **OR**
        - Patient has limited resectable local satellite/in-transit recurrence; **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/borderline resectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.*

Uveal Melanoma ‡ [2,19,20,80]

- Patient has metastatic or unresectable disease; **AND**
- Used in combination with ipilimumab

Merkel Cell Carcinoma ‡ [2,4,33,65,193e]

- Used as neoadjuvant treatment; **AND**
    - Used as a single agent; **AND**
        - Patient is a surgical candidate with primary clinical N0 locally advanced disease where curative surgery and curative radiation therapy were originally deemed not feasible; **OR**
        - Patient has primary clinical N+, M0 regional disease with biopsy positive draining nodal basin; **OR**
- Used for M1 disseminated disease; **AND**
    - Used as a single agent; **AND**

First-line therapy ONLY:
▪ Use of nivolumab will be restricted to patients with a contraindication or intolerance to retifanlimab; **OR**

- Used in combination with ipilimumab; **AND**
  - Used for disease that is refractory to PD-1 therapy; **OR**
- Used for recurrent in-transit N+ regional disease; **AND**
  - Curative surgery and curative radiation therapy (RT) are not feasible; **AND**
    - Used as a single agent; **AND**

First-line therapy ONLY:
– Use of nivolumab will be restricted to patients with a contraindication or intolerance to retifanlimab; **OR**

    - Used in combination with ipilimumab; **AND**
      - Used for disease that is refractory to PD-1 therapy; **OR**
- Used for recurrent N+ regional disease; **AND**
  - Curative surgery and curative radiation therapy (RT) are not feasible; **AND**
    - Used as a single agent; **AND**

First-line therapy ONLY:
– Use of nivolumab will be restricted to patients with a contraindication or intolerance to retifanlimab; **OR**

    - Used in combination with ipilimumab; **AND**
      - Used for disease that is refractory to PD-1 therapy

Peritoneal Mesothelioma (PeM)* ‡ [2,64,90]

- Used as a single agent or in combination with ipilimumab as subsequent therapy (if platinum chemotherapy was administered first-line); **OR**
- Used in combination with ipilimumab as first-line therapy; **AND**
  - Patient has medically inoperable disease and/or complete cytoreduction not achievable, or presence of any high-risk features**; **OR**
  - Patient has disease progression following CRS + HIPEC if no prior adjuvant systemic therapy was given

**Note: May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma.*

***High-risk features include: biphasic/sarcomatoid histology, nodal metastasis, Ki-67 >9%, thrombocytosis, PS=2, bicavitary disease, high disease burden/incomplete cytoreduction (Peritoneal Cancer Index [PCI] >17), completeness of cytoreduction (cc) score >1)*

Pleural Mesothelioma (PM)* † ‡ Φ [1,2,37,38,47,64,81]

- Used as a single agent or in combination with ipilimumab as subsequent therapy (if platinum chemotherapy was administered first-line); **OR**
- Used in combination with ipilimumab; **AND**
  - Used as first-line therapy; **AND**
    - Disease is medically inoperable or unresectable; **OR**
  - Used as induction therapy prior to surgical exploration; **AND**
    - Patient has clinical stage I disease and epithelioid histology

**Note: May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma.*

Non-Small Cell Lung Cancer (NSCLC) † ‡ [1,2,11,22,23,43,45,46,120,43e-45e,51e-53e,56e,125e,127e,166e,190e-192e]

- Patient has resectable (tumors ≥ 4 cm or node positive) disease; **AND**
  - Patient has no known EGFR mutations or ALK rearrangements; **AND**
  - Used as neoadjuvant therapy in combination with platinum-doublet chemotherapy (e.g., cisplatin/carboplatin in combination with paclitaxel, pemetrexed, or gemcitabine) with the option of continuing single-agent nivolumab as adjuvant treatment after surgery; **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; **AND**
    - Used for one of the following:
      - Patients who have tumors that are negative for actionable molecular biomarkers** (may be KRAS G12C mutation positive)
      - Patients who are positive for one of the following molecular biomarkers: EGFR exon 20, KRAS G12C, BRAF V600E, NTRK1/2/3 gene fusions, MET exon 14 skipping, ERBB2 (HER2), or NRG1 gene fusion; **AND**
    - Used in combination with one of the following:
      - Ipilimumab
      - Ipilimumab 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.); **AND**

Squamous NSCLC:

- Use of nivolumab in combination with ipilimumab (with or without platinum-doublet chemotherapy) will be restricted to patients with a contraindication or intolerance to cemiplimab/paclitaxel/(carboplatin or cisplatin); **OR**

Nonsquamous NSCLC:

- Use of nivolumab in combination with ipilimumab (with or without platinum-doublet chemotherapy) will be restricted to patients with a contraindication or intolerance to cemiplimab/(paclitaxel or pemetrexed)/(carboplatin or cisplatin); **OR**

- Used as subsequent therapy; **AND**
  - Used as a single agent; **OR**
  - Used for one of the following:
    - Patients who are positive for one of the following molecular biomarkers and have received prior targeted therapy**§**: EGFR S768I, L861Q, and/or G719X
    - Patients who are positive for one of the following molecular biomarkers: BRAF V600E, NTRK1/2/3 gene fusions, or MET exon 14 skipping; **AND**
  - Used in combination with one of the following:
    - Ipilimumab
    - Ipilimumab 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.); **AND**

Squamous NSCLC:

- Use of nivolumab in combination with ipilimumab (with or without platinum-doublet chemotherapy) will be restricted to patients with a contraindication or intolerance to cemiplimab/paclitaxel/(carboplatin or cisplatin); **OR**

Nonsquamous NSCLC:

- Use of nivolumab in combination with ipilimumab (with or without platinum-doublet chemotherapy) will be restricted to patients with a contraindication or intolerance to cemiplimab/(paclitaxel or pemetrexed)/(carboplatin or cisplatin); **OR**

- Used as continuation maintenance therapy in combination with ipilimumab; **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, NRG1, and ERBB2 (HER2). Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, NRG1, 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.
§ Genomic Aberration/Mutational Driver Targeted Therapies: Refer to guidelines for appropriate use.

Pediatric Aggressive Mature B-Cell Lymphomas – Primary Mediastinal Large B-Cell Lymphoma (PMBCL) ‡ [2,74-76]

- Patient is ≤ 18 years of age*; **AND**
- Used in combination with brentuximab vedotin; **AND**
- Used after autologous stem-cell transplant OR if ineligible for autologous stem-cell transplant, used after 2 or more prior lines of therapy; **AND**
  - Used for relapsed or refractory disease; **OR**
  - Used as consolidation/additional therapy if a partial response was achieved after therapy for relapsed or refractory disease

** Pediatric Primary Mediastinal Large B-Cell Lymphoma may be applicable to adolescent and young adult (AYA) patients <39 years who are treated in a pediatric oncology setting.*

Small Bowel Adenocarcinoma ‡ [2,31,39,59,194e]

- Used as a single agent or in combination with ipilimumab; **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 for advanced or metastatic disease; **AND**
    - Used as primary treatment; **OR**
    - Used as subsequent treatment; **AND**
      - Disease progressed following treatment with a fluoropyrimidine-, oxaliplatin-, and/or irinotecan-based chemotherapy, unless contraindicated; **OR**
  - Used for locally unresectable or medically inoperable disease; **AND**
      - Used as primary treatment; **OR**
- Patient has polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype [e.g., tumor mutational burden (TMB) > 50 mut/Mb] as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Used as single agent; **AND**
  - Used as subsequent therapy for advanced or metastatic disease

Small Cell Lung Cancer (SCLC) ‡ Φ [2,24,61,149e]

- Used as subsequent systemic therapy as a single agent for relapsed or progressive disease; **AND**

• Patient must demonstrate an inadequate response to topotecan or irinotecan, unless there is a contraindication or intolerance, prior to approval of nivolumab

Soft Tissue Sarcoma ‡ [2,72,84,236e,242e]

- Extremity/Body Wall* or Head/Neck*
  - Used as subsequent therapy for advanced/metastatic disease with disseminated metastases; **AND**
    - Patient has myxofibrosarcoma, undifferentiated pleomorphic sarcoma (UPS), dedifferentiated liposarcoma, or undifferentiated sarcomas; **AND**
      - Used in combination with ipilimumab; **AND**

– Use of nivolumab in combination with ipilimumab will be restricted to patients with a contraindication or intolerance to pembrolizumab; **OR**

    - Patient has cutaneous angiosarcoma; **AND**
      - Used in combination with ipilimumab
- Retroperitoneal/Intra-Abdominal**
  - Used as one of the following:
    - Alternative systemic therapy for unresectable or progressive disease after initial therapy for unresectable localized disease; **OR**
    - Palliative subsequent therapy for stage IV disease with disseminated metastases; **AND**
  - Used for one of the following:
    - Patient has myxofibrosarcoma, undifferentiated pleomorphic sarcoma (UPS), dedifferentiated liposarcoma, or undifferentiated sarcomas; **AND**
      - Used in combination with ipilimumab; **AND**

– Use of nivolumab in combination with ipilimumab will be restricted to patients with a contraindication or intolerance to pembrolizumab; **OR**

    - Patient has cutaneous angiosarcoma; **AND**
      - Used in combination with ipilimumab
- Angiosarcoma

- Used in combination with ipilimumab; **AND**

○ Patient must demonstrate an inadequate response to a generically available agent/regimen (e.g., paclitaxel, doxorubicin, etc. *[see NCCN Soft Tissue Sarcoma guideline for complete list of alternatives]*), unless there is a contraindication or intolerance prior to approval of nivolumab; **OR**

- Dedifferentiated Liposarcoma with or without Concurrent Well-Differentiated Liposarcoma
  - Used as in combination with ipilimumab; **AND**

○ Patient must demonstrate a contraindication or intolerance to a generic chemotherapy regimen (e.g., anthracycline-based or gemcitabine-based regimen, etc. [*see NCCN Soft Tissue Sarcoma guidelines for complete list of alternatives*]) prior to approval of nivolumab

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

***For well-differentiated liposarcoma (WDLPS-retroperitoneum, paratesticular) with or without evidence of de-differentiation, treat as other soft tissue sarcomas*

Vulvar Cancer ‡ [2,49]

- Used as a single agent; **AND**
- Used as subsequent therapy for HPV-related advanced, recurrent, or metastatic disease

Vaginal Cancer ‡ [2,49,97]

- Used as subsequent therapy as a single agent; **AND**
- Patient has recurrent or metastatic disease; **AND**
- Tumor expresses PD-L1 (e.g., CPS ≥1) as determined by an FDA-approved or CLIA-compliant test❖

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) ‡ [2,220e]

- Patient has histologic (Richter) transformation to diffuse large B-cell lymphoma; **AND**
- Used in combination with ibrutinib; **AND**
  - Patient is positive for del(17p)/TP53 mutation; **OR**
  - Patient is chemotherapy refractory or unable to receive chemoimmunotherapy

Squamous Cell Skin Cancer ‡ [2,129,130]

- Used as a single agent; **AND**

- Patient has locally advanced disease; **AND**
  - Used as primary treatment if curative surgery and curative radiation therapy (RT) are not feasible; **OR**
- Patient has regional disease that is unresectable, inoperable, or incompletely resected if curative RT is not feasible; **AND**
  - Used as first-line therapy; **OR**
- Patient has satellitosis/in-transit metastasis that is unresectable or incompletely resected; **AND**
  - Used as first-line therapy; **OR**
- Patient has regional recurrence or distant metastatic disease; **AND**
  - Used as first-line therapy; **AND**

- Use of nivolumab will be restricted to patients with a contraindication or intolerance to cemiplimab

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.

Enhanced Oncology Value (EOV) Program – Redacted indications

Uses not listed above have inadequate data to support efficacy and are excluded from prior authorization validity.

Other treatment options including, but are not limited to, the following may be appropriate: radiation therapy, surgery, traditional chemotherapy (e.g., platinum, taxane), compassionate use/expanded access programs, clinical trials, supportive care, integrative and complementary therapies.

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

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

IV. Renewal Criteria Δ 1,2,4-6,15-42,43,47,49,50,52-54,68,72,73,79,81,82,89

Prior authorization validity 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**
- Duration of authorization has not been exceeded *(refer to Section I)*; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion-related reactions, complications of allogeneic hematopoietic stem cell transplantation (HSCT), severe immune-mediated adverse reactions (e.g., pneumonitis, colitis, hepatitis/hepatotoxicity, endocrinopathies, nephritis/renal dysfunction, adverse skin reactions/rash, etc.), etc.; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

Δ Notes:

- Patients responding to therapy who relapse ≥ 6 months after discontinuation due to duration (i.e., receipt of 24 months of therapy) are eligible to re-initiate PD-directed therapy.
- Patients previously presenting with aggressive disease who are exhibiting stable disease on treatment as their best response (or if therapy improved performance status) may be eligible for continued therapy beyond the 24-month limit without interruption or discontinuation.
- Patients who complete adjuvant therapy and progress ≥ 6 months after discontinuation are eligible to re-initiate PD-directed 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 PD-directed therapy and will be evaluated on a case-by-case basis.

V. Dosage/Administration Δ 1,4-6,19,20,27,24,31-42,48-50,52-54,55,58,59,61,65,67,68,71-87,89,91,93,96,98-119,121-124,127-132

Indication	Dose
Ampullary Adenocarcinoma	Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then 3 mg/kg every 2 weeks, or 240 mg every 2 weeks, or 480 mg every 4 weeks until disease progression or unacceptable toxicity
Anal Cancer	Administer 240 mg intravenously every 2 weeks, 480 mg intravenously every 4 weeks, or 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity

Biliary Tract Cancers	Subsequent therapy: • Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years
Urothelial Carcinoma (Bladder Cancer)	First-line therapy: • Administer 360 mg intravenously every 3 weeks for up to 6 cycles (given in combination with gemcitabine and cisplatin), followed by a single-agent maintenance dose of 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity for up to 2 years Disease progression or second-line treatment: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity Adjuvant treatment: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease recurrence or unacceptable toxicity for up to 1 year
Bone Cancer	Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years
Adult CNS Cancers	In combination with ipilimumab: • Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then 3 mg/kg intravenously every 2 weeks, or 240 mg intravenously every 2 weeks, or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity
Pediatric CNS Cancers	Administer 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity

Colorectal Cancer (CRC)	Adult patients and for pediatric patients ≥ 12 years and ≥ 40 kg:
	• **Single agent:** Administer 3 mg/kg intravenously every 2 weeks, or 240 mg intravenously every 2 weeks, or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity
	• **In combination with ipilimumab:**
	  ○ Administer 240 mg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), followed by single agent regimen until disease progression or unacceptable toxicity; **OR**
	  ○ Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), followed by single agent regimen until disease progression or unacceptable toxicity
	Pediatric patients ≥ 12 years and < 40 kg:
	• **Single agent:** Administer 3 mg/kg intravenously every 2 weeks or 6 mg/kg every 4 weeks until disease progression or unacceptable toxicity
	• **In combination with ipilimumab:** Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day),

	followed by single agent regimen until disease progression or unacceptable toxicity.
Appendiceal Adenocarcinoma	• **Single agent:** Administer 3 mg/kg intravenously every 2 weeks, or 240 mg intravenously every 2 weeks, or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity • **In combination with ipilimumab:** ○ Administer 240 mg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), followed by single agent regimen until disease progression or unacceptable toxicity; **OR** ○ Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen until disease progression or unacceptable toxicity
Esophageal and Esophagogastric/ Gastroesophageal Junction Cancer	<u>First line therapy (PD-L1 squamous cell carcinoma)</u> • Administer 240 mg intravenously every 2 weeks or 360 mg intravenously every 3 weeks or 480 mg intravenously every 4 weeks (given in combination with fluoropyrimidine- and platinum-containing chemotherapy) until disease progression or unacceptable toxicity for up to 2 years; **OR** • Administer 3 mg/kg intravenously every 2 weeks or 360 mg intravenously every 3 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years <u>First line therapy (PD-L1 adenocarcinoma)</u> • Administer 240 mg intravenously every 2 weeks or 360 mg intravenously every 3 weeks (given in combination with fluoropyrimidine- and platinum-containing chemotherapy) until disease progression or unacceptable toxicity for up to 2 years <u>Subsequent therapy (PD-L1 squamous cell carcinoma):</u> • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks as a single agent until disease progression or unacceptable toxicity <u>Neoadjuvant/perioperative therapy (MSI-H/dMMR adenocarcinoma):</u> • Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) for 12 weeks, followed by surgery and then post-operative therapy *(See below)* <u>Post-operative therapy (MSI-H/dMMR adenocarcinoma):</u> • Administer 480 mg intravenously every 4 weeks for 36 weeks (9 doses) <u>Adjuvant therapy following neoadjuvant chemoradiotherapy (adenocarcinoma and squamous carcinoma):</u> • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity for up to 1 year
Gastric Cancer	<u>First-line therapy:</u>

	• Administer 240 mg intravenously every 2 weeks or 360 mg intravenously every 3 weeks (give in combination with oxaliplatin and either fluorouracil or capecitabine) until disease progression or unacceptable toxicity for up to 2 years Neoadjuvant/perioperative therapy: • Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) for 12 weeks, followed by surgery and then post-operative therapy *(See below)* Post-operative therapy: • Administer 480 mg intravenously every 4 weeks for 36 weeks (9 doses)
Gestational Trophoblastic Neoplasia (GTN)	In combination with ipilimumab: Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity
SCCHN	Single agent: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with cetuximab: • Administer 240 mg intravenously every 2 weeks until disease progression or unacceptable toxicity
Hepatocellular Carcinoma (HCC)	In combination with ipilimumab: • Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity for up to 2 years
Adult cHL	Single agent: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with brentuximab vedotin • Administer 3 mg/kg intravenously every 3 weeks for up to 24 weeks (8 doses) In combination with ICE (ifosfamide, carboplatin, and etoposide) • Administer 240 mg intravenously every 2 weeks for up to 12 weeks (6 doses) In combination with AVD (doxorubicin, vinblastine, dacarbazine) • Administer 240 mg intravenously every 2 weeks for up to 24 weeks (12 doses)
Pediatric cHL	Single agent: • Administer 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity (*Note: There is no pediatric data for this regimen*) In combination with brentuximab vedotin-based therapy • Administer 3 mg/kg intravenously every 3 weeks for up to 12 weeks (4 doses) In combination with ICE (ifosfamide, carboplatin, and etoposide) • Administer 240 mg intravenously every 2 weeks for up to 12 weeks (6 doses) (*Note: There is no pediatric data for this regimen*)

	<u>In combination with AVD (doxorubicin, vinblastine, dacarbazine)</u> • Patients ≥ 18 years of age: Administer 240 mg intravenously every 2 weeks for up to 24 weeks (12 doses) • Patients 12 to 17 years of age: Administer 3 mg/kg (up to 240 mg max) every 2 weeks for up to 24 weeks (12 doses)
Kaposi Sarcoma	<u>In combination with ipilimumab:</u> • Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years
Renal Cell Carcinoma (RCC)	<u>Single agent:</u> • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity <u>In combination with ipilimumab:</u> • Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen until disease progression or unacceptable toxicity <u>In combination with cabozantinib (Cabometyx):</u> • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity for up to 2 years

Pleural Mesothelioma (PM) & Peritoneal Mesothelioma (PeM) *(including pericardial mesothelioma and tunica vaginalis testis mesothelioma)*	<u>Single agent:</u>
	• Administer 3 mg/kg intravenously or 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity
	<u>In combination with ipilimumab:</u>
	• Subsequent therapy
	  ○ Administer 3 mg/kg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity; **OR**
	  ○ Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity
	• All other lines of therapy:
	  ○ Administer 360 mg intravenously every 3 weeks or 3 mg/kg every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years

Cutaneous Melanoma	<u>Adult patients and pediatric patients ≥ 12 years and ≥ 40 kg:</u> Single agent • <u>Unresectable or metastatic disease:</u> Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity

	• Adjuvant treatment: Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease recurrence or unacceptable toxicity for up to 1 year In combination with ipilimumab • Unresectable or metastatic disease: Administer 1 mg/kg intravenously or 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen • Adjuvant treatment: Administer 1 mg/kg intravenously or 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day) • Neoadjuvant treatment: Administer 3 mg/kg intravenously every 3 weeks for up to 2 doses (given in combination with ipilimumab on the same day) Pediatric patients ≥ 12 years and < 40 kg: Single agent • Unresectable or metastatic disease: Administer 3 mg/kg intravenously every 2 weeks or 6 mg/kg intravenously every 4 weeks until disease progression or unacceptable toxicity • Adjuvant treatment: Administer 3 mg/kg intravenously every 2 weeks or 6 mg/kg intravenously every 4 weeks until disease recurrence or unacceptable toxicity for up to 1 year In combination with ipilimumab • Unresectable or metastatic disease: Administer 1 mg/kg intravenously or 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen • Adjuvant treatment: Administer 1 mg/kg intravenously or 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day)
Uveal Melanoma	In combination with ipilimumab: • Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then 3 mg/kg intravenously every 2 weeks, or 240 mg every 2 weeks, or 480 mg every 4 weeks until disease progression or unacceptable toxicity
Merkel Cell Carcinoma	Neoadjuvant treatment: • Administer 240 mg intravenously every 2 weeks (days 1 and 15) for a total of 2 doses All other settings: Single agent: • Administer 240 mg intravenously every 2 weeks or 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity In combination with ipilimumab:

	• Administer 1 mg/kg intravenously OR 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen; **OR** • Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity
Non-Small Cell Lung Cancer (NSCLC)	Neoadjuvant treatment followed by optional adjuvant treatment: • Administer 360 mg intravenously with platinum-doublet chemotherapy every 3 weeks for up to 4 cycles with the option of continuing single-agent nivolumab as adjuvant treatment after surgery at 480 mg intravenously every 4 weeks for up to 13 cycles or until disease recurrence or unacceptable toxicity Single agent: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with ipilimumab: • Administer 360 mg intravenously every 3 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years; **OR** • Administer 3 mg/kg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years In combination with ipilimumab and platinum-doublet chemotherapy: • Administer 360 mg intravenously every 3 weeks (given in combination with ipilimumab 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.
Pediatric Primary Mediastinal Large B-Cell Lymphoma (PMBCL)	In combination with brentuximab vedotin: Administer 3 mg/kg intravenously, with brentuximab vedotin on day 1, every 2 weeks until disease progression or unacceptable toxicity
Small Bowel Adenocarcinoma	Single agent: • Administer 3 mg/kg intravenously every 2 weeks, or 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with ipilimumab: • Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then 3 mg/kg or 240 mg intravenously every 2 weeks until disease progression or unacceptable toxicity
SCLC	Administer 3 mg/kg intravenously every 2 weeks or 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity
Soft Tissue Sarcoma	In combination with ipilimumab:

	• Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity
Vulvar Cancer, Vaginal Cancer & Cervical Cancer	Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity for up to 2 years
CLL/SLL	In combination with ibrutinib: • Administer 3 mg/kg intravenously every 2 weeks or 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks, until disease progression or unacceptable toxicity
Squamous Cell Skin Cancer	Weight-based dosing: • Administer 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity for up to 1 year **OR** Flat dosing: Administer 240mg intravenously every 2 weeks until disease progression or unacceptable toxicity for up to 2 years

Dosing should be calculated using actual body weight and not flat dosing (as applicable) based on the following:

Frequency (days)	Dosing (mg/kg)	Weight (kg)	Dose (mg)
14	3	<80	220
		<73	200
		<66	180
		<58	160
		<51	140
		<44	120
21	4.5	<80	340
		<78	320
		<73	300
		<68	280
		<63	260
		<58	240
		<53	220
		<48	200
		<44	180
28	6	<80	440
		<77	420
		<73	400

			<69	380	
			<66	360	
			<62	340	
			<58	320	
			<55	300	
			<51	280	
			<47	260	
			<44	240	
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(s):

- Opdivo 40 mg/4 mL single-dose vial: 00003-3772-xx
- Opdivo 100 mg/10 mL single-dose vial: 00003-3774-xx
- Opdivo 120 mg/12 mL single-dose vial: 00003-3756-xx
- Opdivo 240 mg/24 mL single-dose vial: 00003-3734-xx

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Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority

Cost of drug	Yes: Consider for PA

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
C00.9	Malignant neoplasm of lip, unspecified
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
C05.8	Malignant neoplasm of overlapping sites of palate
C05.9	Malignant neoplasm of palate, unspecified

C06.0	Malignant neoplasm of cheek mucosa
C06.2	Malignant neoplasm of retromolar area
C06.80	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
C10.0	Malignant neoplasm of vallecula
C10.1	Malignant neoplasm of anterior surface of epiglottis
C10.2	Malignant neoplasm of lateral wall of oropharynx
C10.3	Malignant neoplasm of posterior wall of oropharynx
C10.4	Malignant neoplasm of branchial cleft
C10.8	Malignant neoplasm of overlapping sites of oropharynx
C10.9	Malignant neoplasm of oropharynx, unspecified
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
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
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
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
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

C22.1	Intrahepatic bile duct carcinoma
C22.3	Angiosarcoma of liver
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
C24.1	Malignant neoplasm of ampulla of Vater
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
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
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
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
C45.1	Mesothelioma of peritoneum
C45.2	Mesothelioma of pericardium
C45.7	Mesothelioma of other sites
C45.9	Mesothelioma, unspecified
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
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 shoulder
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
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
C51.0	Malignant neoplasm of labium majus
C51.1	Malignant neoplasm of labium minus
C51.2	Malignant neoplasm of clitoris
C51.8	Malignant neoplasm of overlapping sites of vulva
C51.9	Malignant neoplasm of vulva, unspecified
C52	Malignant neoplasm of vagina
C53.0	Malignant neoplasm of endocervix

C53.1	Malignant neoplasm of exocervix
C53.8	Malignant neoplasm of overlapping sites of cervix uteri
C53.9	Malignant neoplasm of cervix uteri, unspecified
C58	Malignant neoplasm of placenta
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
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
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C72.9	Malignant neoplasm of central nervous system, unspecified
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
C79.31	Secondary malignant neoplasm of brain
C79.89	Secondary malignant neoplasm of other specified sites
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
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
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
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face, and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes

C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.30	Diffuse large B-cell lymphoma, unspecified site
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32	Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.33	Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
C83.34	Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36	Diffuse large B-cell lymphoma, intrapelvic lymph nodes
C83.37	Diffuse large B-cell lymphoma, spleen
C83.38	Diffuse large B-cell lymphoma, lymph nodes of multiple sites
C83.39	Diffuse large B-cell lymphoma, extranodal and solid organ sites
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
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
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
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
D39.2	Neoplasm of uncertain behavior of placenta
O01.9	Hydatidiform mole, unspecified
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.01	Personal history of malignant neoplasm of esophagus
Z85.028	Personal history of other malignant neoplasm of stomach
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.09	Personal history of malignant neoplasm of other digestive organs
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.12	Personal history of malignant neoplasm of trachea
Z85.51	Personal history of malignant neoplasm of bladder
Z85.59	Personal history of malignant neoplasm of other urinary tract organ
Z85.71	Personal history of Hodgkin lymphoma
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
Z85.841	Personal history of malignant neoplasm of brain
Z85.848	Personal history of malignant neoplasm of other parts of nervous 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		
Jurisdictio	**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 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