Nivolumab (Intravenous)

NDC CODE(S) 00003-3772-XX OPDIVO 10MG/ML Solution (B-M SQUIBB U.S. (PRIMARY CARE)
00003-3774-XX OPDIVO 100MG/10ML Solution (B-M SQUIBB U.S. (PRIMARY CARE)
00003-3734-XX OPDIVO 240MG/24ML Solution (B-M SQUIBB U.S. (PRIMARY CARE)

DESCRIPTION

Nivolumab is a human monoclonal antibody classified as an IgG4 kappa immunoglobulin. It blocks the interaction with PD-1, programmed death receptor-1, and its ligands PD-L1 and PD-L2. When the PD-1 receptor found on T-cells binds with its ligands, T-cell proliferation and cytokine production is inhibited. Some tumors cause increased production of PD-1 ligands and can contribute to the inhibition of active T-cell immune surveillance of tumors. Nivolumab releases pathway-mediated inhibition of the immune response, including the anti-tumor immune response, which results in decreased tumor growth

POLICY

- Nivolumab for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met: **(See Medical Appropriateness below.)**
  - Anal Carcinoma
  - Central Nervous System Cancer
  - Colorectal Cancer (CRC)
  - Endometrial Carcinoma (Uterine Neoplasms)
  - Esophageal Squamous Cell Carcinoma
  - Extranodal NK/ T-Cell Lymphoma
  - Gestational Trophoblastic Neoplasia
  - Hepatocellular Carcinoma (HCC)
  - Hodgkin lymphoma
  - Malignant Pleural Mesothelioma
  - Melanoma, Cutaneous
  - Melanoma, Uveal
  - Merkel Cell Carcinoma
  - Non-small cell lung cancer (NSCLC)
  - Renal cell carcinoma (i.e., kidney cancer)
  - Small bowel adenocarcinoma (SBA)
  - Small cell lung cancer (SCLC)
  - Squamous cell carcinoma of the head and neck
  - Urothelial carcinoma (Bladder Cancer)
  - Vulvar Cancer (Squamous Cell Carcinoma)
- Nivolumab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Nivolumab is considered **medically appropriate** if **ALL** of the following criteria are met:
  - Individual is 18 years of age or older (unless otherwise specified)

- Individual has not received previous therapy with a programmed death ligand (PD-1/PD-L1)-directed therapy (e.g., cemiplimab, avelumab, pembrolizumab, atezolizumab, durvalumab, etc.) prior to initiation of therapy unless otherwise specified
- Diagnosis of **ANY ONE** of the following:
  - Anal Carcinoma if **ALL** of the following:
    - Individual has metastatic squamous cell disease
    - Used as a single agent for subsequent therapy
  - Central Nervous System Cancer if **ALL** of the following:
    - Used for the treatment of brain metastases in individuals with **ANY ONE** of the following:
      - Melanoma and used as a single agent or in combination with ipilimumab for the treatment of brain metastases
      - PD-L1 positive non-small cell lung cancer (NSCLC) and used as a single-agent for the treatment of brain metastases
    - Used in **ANY ONE** of the following treatment settings:
      - Used as initial treatment in individuals with small asymptomatic brain metastases
      - Used for relapsed disease in individuals with limited brain metastases and stable systemic disease or reasonable treatment options
      - Individual has recurrent limited brain metastases
      - Used for recurrent disease in individuals with extensive brain metastases and stable systemic disease or reasonable systemic treatment options
  - Colorectal cancer (CRC) if **ALL** of the following:
    - Individual is 12 years of age or older
    - Disease must be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)
    - Used as **ANY ONE** of the following:
      - Used as a single agent or in combination with ipilimumab as subsequent therapy for advanced or metastatic disease that progressed following treatment with a fluoropyrimidine, oxaliplatin, and/or irinotecan based chemotherapy
      - Used as a single agent or in combination with ipilimumab as primary treatment for unresectable or metastatic disease after previous adjuvant FOLFOX (fluorouracil, leucovorin and oxaliplatin) or CapeOX (capecitabine-oxaliplatin) in the past 12 months
      - Used as single agent as primary treatment for unresectable or metastatic disease in individuals who are not candidates for intensive therapy
      - Used as a single agent for unresectable or metastatic disease that remains unresectable after primary treatment in individuals who are not candidates for intensive therapy
  - Endometrial Carcinoma (Uterine Neoplasms) and **ALL** of the following:
    - Used as a single agent
    - Used as second-line therapy for mismatch repair deficient (dMMR) recurrent, metastatic, or high-risk disease
  - Extranodal NK/ T-Cell Lymphoma and **ALL** of the following:
    - Used as a single agent for relapsed or refractory nasal type disease
    - Disease progressed following additional treatment with an alternative asparaginase-based chemotherapy regimen not previously used
    - Participation in a clinical trial is unavailable
  - Esophageal Squamous Cell Carcinoma and **ALL** of the following:
    - Used as a single agent
    - Used as subsequent therapy for unresectable advanced (or is not a surgical candidate) recurrent, or metastatic disease
  - Gestational Trophoblastic Neoplasia used as a single agent for multiagent chemotherapy resistant disease and **ANY ONE** of the following:

- Recurrent or progressive disease and has intermediate placental site trophoblastic or epithelioid trophoblastic tumor and was previously treated with a platinum/etoposide-containing regimen
- Individual has methotrexate-resistant high-risk disease (i.e., FIGO stages II-III and ≥7 Prognostic score OR FIGO stage IV disease)

▪ Hepatocellular Carcinoma (HCC) if **ALL** of the following:
- Individual has locally advanced, unresectable, inoperable, or metastatic disease~~.~~
- Used as subsequent therapy and **ANY ONE** of the following:
  - Individual has Child-Pugh Class A or B~~7~~ disease and used as a single agent
  - Individual has Child-Pugh Class A disease and used in combination with ipilimumab

▪ Hodgkin lymphoma (cHL) classified as classical disease (cHL) and **ANY ONE** of the following:
- Used as a single agent for **ANY ONE** of the following:
  - Individual is 18 years of age or younger and **ALL** of the following:
    - Used as subsequent therapy for relapsed or refractory disease
    - Used in individuals heavily pretreated (with platinum or anthracycline-based chemotherapy) or if a decrease in cardiac function is observed
  - Individual is 18 years of age or older and has received 2 or more prior lines of therapy or used as palliative therapy in individuals more than 60 years old and **ANY ONE** of the following:
    - Individual has relapsed or progressive disease after an autologous hematopoietic stem cell transplantation (HSCT) with or without brentuximab vedotin
    - Individual has relapsed or refractory disease and is either transplant -ineligible based on comorbidities or has failure of second-line chemotherapy
    - Individual is post allogeneic stem-cell transplant
- Used in combination with brentuximab vedotin for relapsed or refractory disease and **ANY ONE** of the following:
  - Individual is 18 years of age or younger as **ANY ONE** of the following:
    - Used as subsequent therapy for relapsed or refractory disease in individuals heavily pretreated (with platinum or anthracycline-based chemotherapy) or if a decrease in cardiac function is observed
    - Used as re-induction therapy for **ANY ONE** of the following:
      - Used in individuals heavily pretreated (with platinum or anthracycline-based chemotherapy) or if a decrease in cardiac function is observed
      - Used with radiation therapy (ISRT) in highly favorable individuals 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)
  - Individual is 18 years of age or older and used as subsequent therapy (if not previously used)

▪ Malignant Pleural Mesothelioma used as **ANY ONE** of the following:
- Single agent or in combination with ipilimumab as subsequent therapy
- Combination with ipilimumab as first-line therapy in individuals with unresectable disease

▪ Melanoma, cutaneous if **ANY ONE** of the following:
- Used as first line therapy for unresectable or metastatic disease and used as a single agent or in combination with ipilimumab
- Used as subsequent therapy for unresectable or metastatic* disease for **ANY ONE** of the following:
  - Used for retreatment of disease as re-induction as a single agent or in combination with ipilimumab in individuals 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
  - Used after disease progression on first-line therapy or maximum clinical benefit from BRAF-targeted therapy (e.g., dabrafenib/trametinib, vemurafenib/cobimetinib, encorafenib/binimetinib, etc.) for **ANY ONE** of the following:

        - Used as a single agent or in combination with ipilimumab if checkpoint inhibitor immunotherapy was not previously used
        - Used in combination with ipilimumab for individuals who progressed on single agent checkpoint inhibitor immunotherapy
    - Used as adjuvant treatment as a single agent and **ANY ONE** of the following:
        - Individual has lymph node involvement and has undergone complete resection, complete lymph node dissection (CLND), therapeutic lymph node dissection (TLND), or nodal basin ultrasound surveillance
        - Individual has satellite/in-transit metastases or recurrence and has no evidence of disease after complete excision
        - Individual has undergone TLND and/or complete resection of nodal recurrence
        - Individual has undergone complete resection of distant metastatic disease

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

- Melanoma, Uveal and **ALL** of the following:
    - Individual has distant metastatic disease
    - Used as a single agent or in combination with ipilimumab
- Merkel Cell Carcinoma if **ALL** of the following:
    - Used as a single agent
    - Individual has disseminated metastatic disease
- Non-Small Cell Lung Cancer (NSCLC) if **ANY ONE** of the following:
    - Individual has metastatic disease with high tumor mutational burden (TMB)** (i.e., ≥10 mutations per megabase) and used as single agent or in combination with ipilimumab as first-line therapy
    - 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 **ANY ONE** of the following:
        - Used as first-line therapy in combination with ipilimumab OR in combination with ipilimumab and platinum-doublet chemotherapy (e.g., pemetrexed and either carboplatin or cisplatin for non-squamous cell histology, paclitaxel and carboplatin for squamous cell histology, etc.) and **ANY ONE** of the following:
            - Used in individuals with PS 0-1 who have EGFR, ALK, ROS1, BRAF, MET exon skipping mutation, and RET rearrangement negative*** tumors and PD-L1 expression <1%
            - Used in individuals with PS 0-1 who are positive for one of the following molecular biomarkers: BRAF V600E mutations, NTRK gene fusions, MET exon 14 skipping mutations, or RET rearrangements
            - Used in individuals with PS 0-2 for PD-L1 expression-positive (PD-L1≥1%) tumors, as detected by an FDA or CLIA compliant test (If confirmed using an immunotherapy assay-http://www.fda.gov/CompanionDiagnostics) that are EGFR, ALK, ROS1, BRAF, MET exon skipping mutation, and RET rearrangement negative***
        - Used as subsequent therapy and **ANY ONE** of the following:
            - Used as a single agent
            - Used in combination with ipilimumab OR in combination with ipilimumab, pemetrexed, and either carboplatin or cisplatin for non-squamous cell histology OR in combination with ipilimumab, paclitaxel, and carboplatin for squamous cell histology for **ANY ONE** of the following:
                - In individuals with PS 0-1 who have EGFR, ALK, or ROS1,positive tumors and have received prior targeted therapy****

- In individuals with PS 0-1 who are positive for one of the following molecular biomarkers: BRAF V600E mutations, NTRK gene fusions, MET exon 14 skipping mutations, or RET rearrangements

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

*** If there is insufficient tissue to allow testing for all of the EGFR, ALK, ROS1, BRAF, MET, and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.

- Renal cell carcinoma (RCC) (i.e., kidney cancer) if **ANY ONE** of the following:
  - Used in combination with ipilimumab for clear cell histology and **ANY ONE** of the following:
    - Used as first-line therapy in individuals with advanced, relapsed, or stage IV disease with intermediate or poor risk
    - Used as first-line therapy in individuals with relapsed or stage IV disease with favorable risk
    - Used as subsequent therapy in individuals with relapsed or stage IV disease
  - Used as a single agent for **ANY ONE** of the following:
    - Used as subsequent therapy in individuals with advanced, relapsed, or stage IV disease for clear cell histology
    - Individual has relapsed or stage IV disease and non-clear cell histology
- Small bowel adenocarcinoma (SBA) if **ALL** of the following:
  - Individual has advanced or metastatic disease that is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)
  - Used as single agent or in combination with ipilimumab (in one of the following settings) for **ANY ONE** of the following:
    - As subsequent therapy
    - As initial therapy in individuals with prior oxaliplatin exposure in the adjuvant setting or contraindication.
- Small cell lung cancer (SCLC) and used as subsequent systemic therapy for **ANY ONE** of the following:
  - Single agent therapy for metastatic disease with progression after platinum-based treatment and at least one other line of therapy
  - Treatment as single agent and **ANY ONE** of the following:
    - Used for relapse within 6 months following complete response, partial response or stable disease with initial treatment and individual did not relapse while on maintenance atezolizumab or durvalumab
    - Used for primary progressive disease
- Squamous cell carcinoma of the head and neck (SCCHN) if **ALL** of the following:
  - Single agent therapy
  - Recurrent, unresectable, persistent or metastatic disease
  - Disease progression on or after platinum-based therapy
  - Individual does not have nasopharyngeal disease
- Urothelial carcinoma (Bladder Cancer) if **ALL** of the following:
  - Used as a single agent
  - Used as subsequent systemic therapy after previous platinum treatment (see Note)
  - Individual has-**ANY ONE** of the following diagnoses:
    - Locally advanced or metastatic urothelial carcinoma
    - Local bladder cancer recurrence or persistent disease in a preserved bladder
    - Local or metastatic bladder cancer recurrence post-cystectomy
    - Recurrent or metastatic primary carcinoma of the urethra and Individual does not have recurrence of stage T3-4 disease or palpable inguinal lymph nodes
    - Metastatic upper genitourinary (GU) tract tumors
    - 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.

▪ Vulvar Cancer (Squamous Cell Carcinoma) and **ALL** of the following:

- Used as a single agent
- Used as second-line therapy for HPV-related advanced, recurrent, or metastatic disease

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

RET rearrangement-positive tumors • Cabozantinib • Selpercatinib • Vandetanib

RENEWAL CRITERIA

- Nivolumab is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
  - Individual continues to meet initial approval criteria (not including prerequisite therapy)
  - Disease response with treatment defined as stabilization of disease or decrease in size of tumor or tumor spread
  - Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: 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.
  - Additional requirements for diagnoses of **ANY ONE** of the following:
    - NSCLC (in combination with ipilimumab or in combination with ipilimumab and two (2) cycles of platinum-doublet chemotherapy) and individual has not exceeded a maximum of two (2) years of therapy
    - Melanoma, cutaneous adjuvant treatment has not exceeded a maximum of twelve (12) months of therapy
    - Melanoma, cutaneous Re-induction – Refer to initial criteria
    - Malignant Pleural Mesothelioma (MPM) (initial therapy in combination with ipilimumab) and individual has not exceeded a maximum of two (2) years of therapy
    - Vulvar Cancer and individual has not exceeded a maximum of two (2) years of therapy

INDICATION(S)	DOSAGE & ADMINISTRATION
Merkel Cell	Administer 240 mg intravenously every 2 weeks or 3 mg/kg intravenously every 2 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.
Cutaneous Melanoma	**Single agent (excluding adjuvant therapy):** • Administer 240 mg intravenously every 2 weeks OR 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity **In combination with ipilimumab (excluding adjuvant therapy):** • Administer 1 mg/kg intravenously, with ipilimumab on the same day, every 3 weeks for 4 doses, then follow with single agent regimen **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
Uveal Melanoma	**Single agent:** • Administer up to 10 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity **In combination with ipilimumab:** • Administer 1 mg/kg intravenously, with ipilimumab on the same day, every 3 weeks for 4 doses, then 3mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity

NSCLC	**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 3 mg/kg intravenously every 2 weeks, with ipilimumab 1 mg/kg every 6 weeks, until disease progression or unacceptable toxicity for up to 2 years **In combination with ipilimumab and platinum-doublet chemotherapy for metastatic or recurrent disease** Administer 360 mg intravenously every 3 weeks, with 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, Esophageal Squamous Cell Carcinoma, and Gestational Trophoblastic Neoplasia (GTN)	Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks, until disease progression or unacceptable toxicity.
MSI-H/dMMR CRC	**Adult patients and for pediatric patients ≥ 12 years and ≥ 40 kg** ▪ **As a 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 3 mg/kg intravenously, with ipilimumab 1 mg/kg on the same day, every 3 weeks for 4 doses, then follow with the single agent regimen **Pediatric patients ≥ 12 years and < 40 kg** ▪ **As a single agent**: Administer 3 mg/kg intravenously every 2 weeks, until disease progression or unacceptable toxicity. ▪ **In combination with ipilimumab:** Administer 3 mg/kg intravenously, with ipilimumab 1 mg/kg on the same day, every 3 weeks for 4 doses, then follow with the single agent regimen
SCLC	• Administer 240 mg intravenously every 2 weeks until disease progression or unacceptable toxicity
Renal Cell Carcinoma (RCC)	**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 3 mg/kg, intravenously with ipilimumab on the same day, every 3 weeks for 4 doses, then follow single-agent regimen
Hepatocellular Carcinoma (HCC)	**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 1 mg/kg intravenously, with ipilimumab on the same day, every 3 weeks for 4 doses, then follow with single-agent regimen
Malignant Pleural Mesothelioma (MPM)	**Single agent:** • Administer 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity **In combination with ipilimumab:** **Subsequent Therapy:**

	• Administer 3 mg/kg intravenously every 2 weeks, with ipilimumab 1mg/kg every 6 weeks, until disease progression or unacceptable toxicity OR • Administer 240 mg every 2 weeks, intravenously with 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 **Initial Therapy:** • Administer 360 mg intravenously every 3 weeks, with ipilimumab 1 mg/kg every 6 weeks; treatment with nivolumab is continued for up to 2 years or until disease progression or unacceptable toxicity
CNS Metastases from Melanoma	**Single agent:** • Administer 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity **In combination with ipilimumab:** • Administer 1 mg/kg intravenously, with ipilimumab on the same day, every 3 weeks for 4 doses, then 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity
CNS Metastases from NSCLC	Administer 3 mg/kg intravenously 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, with ipilimumab on the same day, every 3 weeks for 4 doses, then 3 mg/kg or 240 mg intravenously every 2 weeks until disease progression or unacceptable toxicity
Extranodal NK/ T-Cell Lymphoma	Administer 40 mg intravenously every 2 weeks until disease progression or unacceptable toxicity
Endometrial Carcinoma	Administer 3 mg/kg intravenously every 2 weeks for 8 doses and then 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity
Vulvar Cancer	Administer 240 mg intravenously every 2 weeks; treatment is continued for up to 2 years or until disease progression or unacceptable toxicity
Dosing should be calculated using actual body weight and not flat dosing (as applicable) based on the following: Weight ≥ 74 kg : • Standard dose 480 mg IV every 4 weeks Weight is 67 kg to 73 kg : •Use 440 mg IV every 4 weeks Weight is ≤ 66 kg •Use 400 mg IV every 4 weeks -OR- Weight > 67 kg: • Standard dose 240 mg IV every 2 weeks Weight is 53 kg to 67 kg: •Use 200 mg IV every 2 weeks Weight is < 53kg: •Use 160 mg IV every 2 weeks	
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.*	

LENGTH OF AUTHORIZATION

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

Adjuvant use in the treatment of melanoma can be authorized up to a maximum of 12 months of therapy.

Use in the treatment of NSCLC in combination with ipilimumab can be authorized up to a maximum of 2 years of therapy.

Use in the treatment 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.

Use in the treatment of MPM as initial therapy in combination with ipilimumab can be authorized up to a maximum of 2 years of therapy.

Use in the treatment of Vulvar Cancer can be authorized for up to a maximum of 2 years of therapy.

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

Lexicomp Online. (2020, March). AHFS DI. *Nivolumab*. Retrieved November 16, 2020 from Lexicomp Online with AHFS.

MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, November). *Nivolumab*. Retrieved November 16, 2020 from MICROMEDEX Healthcare Series.

National Comprehensive Cancer Network. (2020). NCCN Drugs & Biologics Compendium®. *Nivolumab*. Retrieved November 12, 2020 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2020). NCCN Drugs & Biologics Compendium (NCCN Guidelines®) Gestational Trophoblastic Neoplasia. Version 3.2020. National Comprehensive Cancer Network, 2020. Retrieved November 17, 2020

National Comprehensive Cancer Network. (2020). NCCN Drugs & Biologics Compendium (NCCN Guidelines®) Pediatric Hodgkin Lymphoma. Version 2.2021. National Comprehensive Cancer Network, 2020. Retrieved November 17, 2020

U. S. Food and Drug Administration. (2020, October). Center for Drug Evaluation and Research. *Opdivo™ nivolumab injection, for intravenous use.* Retrieved November 12, 2020 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125554s072lbl.pdf

EFFECTIVE DATE 4/2/21

ID_MRx