Nivolumab (Opdivo®)

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 or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Unresectable or Metastatic Melanoma
Opdivo, as a single agent or in combination with ipilimumab, is indicated for the treatment of adult and pediatric patients 12 years and older with unresectable or metastatic melanoma.

Adjuvant Treatment of Melanoma
Opdivo is indicated for the adjuvant treatment of adult and pediatric patients 12 years and older with completely resected stage IIB, stage IIC, stage III, or stage IV melanoma.

Metastatic Non-Small Cell Lung Cancer

- Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1 (≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.
- Opdivo, in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy, is indicated for the first-line treatment of adult patients with metastatic or recurrent NSCLC, with no EGFR or ALK genomic tumor aberrations.
- Opdivo is indicated for the treatment of adult patients with metastatic NSCLC with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo.

Neoadjuvant and Adjuvant Treatment of Resectable Non-Small Cell Lung Cancer
Opdivo, in combination with platinum-doublet chemotherapy, is indicated as neoadjuvant treatment of adult patients with resectable (tumors ≥4 cm or node positive) non-small cell lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements, followed by single-agent Opdivo as adjuvant treatment after surgery.

Neoadjuvant Treatment of Resectable Non-Small Cell Lung Cancer
Opdivo, in combination with platinum-doublet chemotherapy, is indicated as neoadjuvant treatment of adult patients with resectable (tumors ≥4 cm or node positive) non-small cell lung cancer (NSCLC).

Malignant Pleural Mesothelioma
Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with unresectable malignant pleural mesothelioma.

Advanced Renal Cell Carcinoma

- Opdivo as a single agent is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.
- Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with intermediate or poor risk advanced RCC.
- Opdivo, in combination with cabozantinib, is indicated for the first-line treatment of adult patients with advanced RCC.

Classical Hodgkin Lymphoma

Opdivo is indicated for the treatment of adult patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after:

- Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
- Three or more lines of systemic therapy that includes autologous HSCT.

Squamous Cell Carcinoma of the Head and Neck

Opdivo is indicated for the treatment of adult patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

Urothelial Carcinoma

- Opdivo is indicated for the adjuvant treatment of adult patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of UC.
- Opdivo, in combination with cisplatin and gemcitabine, is indicated for the first-line treatment of adult patients with unresectable or metastatic urothelial carcinoma.
- Opdivo is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who:
  - Have disease progression during or following platinum-containing chemotherapy.
  - Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Microsatellite Instability-High or Mismatch Repair Deficient Metastatic Colorectal Cancer

- Opdivo, in combination with ipilimumab, is indicated for the treatment of adult and pediatric patients 12 years and older with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC).
- Opdivo, as a single agent, is indicated for the treatment of adult and pediatric patients 12 years and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Hepatocellular Carcinoma

- Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with unresectable or metastatic hepatocellular carcinoma (HCC).
- Opdivo, in combination with ipilimumab, is indicated for the treatment of adult patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Esophageal Carcinoma

- Opdivo is indicated for the adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in adult patients who have received neoadjuvant chemoradiotherapy (CRT).
- Opdivo, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) whose tumors express PD-L1 (≥ 1).

- Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) whose tumors express PD-L1 (≥ 1).
- Opdivo is indicated for the treatment of adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

Gastric Cancer, Gastroesophageal Junction Cancer, Esophageal Adenocarcinoma
Opdivo, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the treatment of adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma whose tumors express PD-L1 (≥ 1).

Compendial Uses

- Cutaneous melanoma
- Non-small cell lung cancer
- Renal cell carcinoma
- Classic Hodgkin lymphoma
- Head and neck cancers
- Urothelial carcinoma
  - Bladder cancer
  - Primary carcinoma of the urethra
  - Upper genitourinary tract tumors
  - Urothelial carcinoma of the prostate
- Colorectal cancer, including anal adenocarcinoma
- Appendiceal neoplasms and cancers
- Small bowel adenocarcinoma
- Ampullary Adenocarcinoma
- Hepatocellular carcinoma
- Uveal Melanoma
- Anal Carcinoma
- Merkel Cell Carcinoma
- Central Nervous System (CNS) brain metastases
- Gestational trophoblastic neoplasia
- Pleural mesothelioma
- Peritoneal mesothelioma
- Extranodal NK/T-cell lymphoma
- Uterine Neoplasms
  - Endometrial Carcinoma
  - Uterine Sarcoma
- Esophageal/Esophagogastric Junction Cancers
- Vulvar Cancer
- Gastric Cancer
- Small cell lung cancer
- Cervical Cancer
- Pediatric Diffuse High-Grade Gliomas
- Pediatric Primary Mediastinal Large B-cell Lymphoma
- Kaposi Sarcoma
- Bone Cancer
- Biliary Tract Cancers

  - Cholangiocarcinoma
  - Gallbladder Cancer
- Soft Tissue Sarcoma
  - Angiosarcoma
  - Dedifferentiated liposarcoma
  - Epithelioid hemangioendothelioma
  - Extremity/body wall sarcoma
  - Head/neck sarcoma
  - Retroperitoneal/intra-abdominal sarcoma
  - Rhabdomyosarcoma
- Anaplastic Thyroid Carcinoma
- Histologic (Richter) transformation to diffuse large B-cell lymphoma
- Vaginal Cancer
- Squamous Cell Skin Carcinoma
- Adrenal Gland Tumors

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- Documentation of laboratory report confirming microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or polymerase epsilon/delta (POLE/POLD1) tumor status, where applicable.
- Documentation of programmed death ligand 1 (PD-L1) tumor expression, where applicable.
- Documentation of the absence of EGFR exon 19 deletion and exon 21 L858R mutations, ALK, RET, and ROS1 gene fusions, where applicable.
- Documentation of human epidermal growth factor receptor 2 (HER2) status, where applicable.

EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor therapy unless any of the following apply:

- The requested medication will be used for treatment of metastatic or unresectable melanoma.
- The requested medication will be used for treatment of metastatic or unresectable small bowel adenocarcinoma in combination with ipilimumab following progression on single agent checkpoint inhibitor therapy.
- The requested medication will be used for treatment of hepatocellular carcinoma following progression on therapy with atezolizumab plus bevacizumab.

COVERAGE CRITERIA

Cutaneous Melanoma

Authorization of 6 months may be granted for treatment of cutaneous melanoma when any of the following apply:

- The requested medication will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent) for unresectable or metastatic disease.
- The requested medication will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent) as adjuvant treatment of stage III or IV disease following complete resection or no evidence of disease.

- The requested medication will be used as single agent adjuvant treatment of stage IIB or IIC disease following wide excision.
- The requested medication will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent) as neoadjuvant treatment.

Non-Small Cell Lung Cancer (NSCLC)

Authorization of 6 months may be granted for treatment of recurrent, advanced, or metastatic non-small cell lung cancer (NSCLC) when both of the following criteria are met:

- There are no EGFR exon 19 deletions, exon 21 L858R mutations, or ALK, RET, or ROS1 gene fusions (unless testing is not feasible due to insufficient tissue).
- The requested medication will be used in a regimen containing ipilimumab or as single agent for subsequent therapy.

Authorization of 3 months (for up to 3 cycles total) may be granted for neoadjuvant treatment of resectable NSCLC in combination with platinum-doublet chemotherapy when there are no known EGFR exon 19 deletions, exon 21 L858R mutations, or ALK, RET, or ROS1 gene fusions (unless testing is not feasible due to insufficient tissue.

Authorization of 6 months may be granted for neoadjuvant and adjuvant treatment of resectable NSCLC when both of the following criteria are met:

- There are no EGFR exon 19 deletions, exon 21 L858R mutations, or ALK, RET, or ROS1 gene fusions (unless testing is not feasible due to insufficient tissue).
- The requested medication will be used in combination with platinum-doublet chemotherapy (for up to 4 cycles total), followed by single agent adjuvant therapy (for up to 13 cycles).

Renal Cell Carcinoma

Authorization of 6 months may be granted for treatment of relapsed, advanced, or stage IV renal cell carcinoma, when any of the following criteria are met:

- The requested medication will be used as a single agent for clear cell histology as subsequent therapy.
- The requested medication will be used as a single agent for non-clear cell histology.
- The requested medication will be used in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent) for disease with clear cell histology.
- The requested medication will be used in combination with cabozantinib.

Classic Hodgkin Lymphoma (cHL)

Authorization of 6 months may be granted for treatment of classic Hodgkin lymphoma when the requested medication will be used in any of the following regimens:

- As a single agent.
- In combination with brentuximab vedotin.
- In combination with ICE (ifosfamide, carboplatin, etoposide).
- In combination with AVD (doxorubicin, vinblastine, and dacarbazine).

Head and Neck Cancers

Authorization of 6 months may be granted for treatment of head and neck cancers in members with either of the following:

- Non-nasopharyngeal very advanced head and neck cancer that is unresectable, recurrent, persistent, or metastatic, in combination with cetuximab or as a single agent.

- Nasopharyngeal cancer in combination with cisplatin and gemcitabine for unresectable, recurrent, persistent, or metastatic disease.

Urothelial Carcinoma – Bladder Cancer

Authorization of 6 months may be granted when used in combination with gemcitabine and cisplatin for up to 6 cycles followed by nivolumab maintenance therapy as first line treatment of bladder cancer.

Authorization of 6 months may be granted as a single agent for treatment of bladder cancer when any of the following conditions are met:

- As subsequent therapy for locally advanced or metastatic disease.
- As adjuvant therapy in members who are at high risk of recurrence after undergoing resection.

Urothelial Carcinoma – Primary Carcinoma of the Urethra

Authorization of 6 months may be granted in combination with gemcitabine and cisplatin for up to 6 cycles followed by nivolumab maintenance therapy as first line treatment of primary carcinoma of the urethra.

Authorization of 6 months may be granted as a single agent for treatment of primary carcinoma of the urethra when either of the following are met:

- As subsequent therapy for recurrent, locally advanced, or metastatic disease.
- As adjuvant therapy in members who are at high risk of recurrence after undergoing resection.

Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate

Authorization of 6 months may be granted in combination with gemcitabine and cisplatin for up to 6 cycles followed by nivolumab maintenance therapy as first line treatment of metastatic upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate.

Authorization of 6 months may be granted as a single agent for treatment of upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate when either of the following are met:

- As subsequent therapy for locally advanced or metastatic disease.
- As adjuvant therapy in members who are at high risk of recurrence after undergoing resection.

Colorectal Cancer

Authorization of 6 months may be granted for treatment of colorectal cancer, including anal adenocarcinoma, for microsatellite-instability high (MSI-H), mismatch repair deficient (dMMR), or polymerase epsilon/delta (POLE/POLD1) tumors with ultra-hypermutated phenotype (e.g., tumor mutational burden (TMB) > 50 mut/Mb) when used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent).

Appendiceal Neoplasms and Cancers

Authorization of 6 months may be granted for treatment of appendiceal neoplasms and appendiceal cancers (including appendiceal adenocarcinoma, goblet cell adenocarcinoma, and undifferentiated carcinoma not otherwise specified) for microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or polymerase epsilon/delta (POLE/POLD1) tumors with ultra-hypermutated phenotype (e.g., tumor mutational burden (TMB) > 50 mut/Mb) when used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent).

Small Bowel Adenocarcinoma

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent) for treatment of unresectable, medically inoperable, advanced, or metastatic small bowel adenocarcinoma for microsatellite-instability high (MSI-H), mismatch repair deficient (dMMR), or polymerase epsilon/delta (POLE/POLD1) tumors with ultra-hypermutated phenotype (e.g., tumor mutational burden (TMB) > 50 mut/Mb).

Ampullary Adenocarcinoma

Authorization of 6 months may be granted in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent) for treatment of progressive or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) ampullary adenocarcinoma.

Hepatocellular Carcinoma

Authorization of 6 months may be granted for treatment of hepatocellular carcinoma for either of the following:

- First-line treatment of unresectable or extrahepatic/metastatic disease in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent).
- Subsequent treatment as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent).

Uveal Melanoma

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent) for treatment of uveal melanoma for unresectable or metastatic disease.

Anal Carcinoma

Authorization of 6 months may be granted as a single agent for subsequent treatment of metastatic anal carcinoma.

Merkel Cell Carcinoma

Authorization of 6 months may be granted for treatment of Merkel cell carcinoma in any of the following settings:

- Metastatic disease.
- In-transit, locally advanced, or regional disease when used as a single agent.
- Unresectable, recurrent, regional, in transit, or stage IV disease when used in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent).

CNS Brain Metastases

Authorization of 6 months may be granted for treatment of CNS brain metastases when either of the following criteria are met:

- The requested medication will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by nivolumab as a single agent) in members with BRAF non-specific melanoma.
- The requested medication will be used as a single agent in members with PD-L1 positive non-small cell lung cancer.

Gestational Trophoblastic Neoplasia

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for treatment of multiagent chemotherapy-resistant gestational trophoblastic neoplasia when either of the following criteria is met:

- Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor).
- Member has high-risk disease.

Pleural or Peritoneal Mesothelioma

Authorization of 6 months may be granted for the treatment of pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma, in either of the following settings:

- The requested medication will be used as first line or induction therapy in combination with ipilimumab.
- The requested medication will be used as subsequent therapy as a single agent or in combination with ipilimumab.

Extranodal NK/T-Cell Lymphoma

Authorization of 6 months may be granted for treatment of relapsed or refractory extranodal NK/T-cell lymphoma.

Uterine Neoplasms

Authorization of 6 months may be granted as a single agent for subsequent treatment of recurrent microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) endometrial carcinoma.

Authorization of 6 months may be granted in combination with ipilimumab for subsequent treatment of recurrent unresectable or metastatic endometrial carcinoma that is tumor mutational burden-high (TMB-H) [≥10 mut/Mb] and has no satisfactory alternative treatment options.

Authorization of 6 months may be granted in combination with ipilimumab for subsequent treatment of unresectable or metastatic uterine sarcoma that is tumor mutational burden-high (TMB-H) [≥10 mut/Mb] and has no satisfactory alternative treatment options.

Esophageal and Esophagogastric Junction Cancer

Authorization of 6 months may be granted for treatment of esophageal or esophagogastric junction cancer in members who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease for either of the following

- First-line therapy when PD-L1 ≥ in combination with ipilimumab or chemotherapy.
- Subsequent therapy.

Authorization of 6 months may be granted for adjuvant treatment of completely resected esophageal or esophagogastric junction cancer with residual pathologic disease.

Authorization of 6 months may be granted as a single agent, in combination with chemotherapy, or in combination with ipilimumab for treatment of esophageal or esophagogastric junction cancer if tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).

Authorization of 6 months may be granted for induction therapy for relieving dysphagia in combination with ipilimumab or chemotherapy for members with esophageal or esophagogastric junction squamous cell carcinoma with PD-L1 ≥ 1 planned for esophagectomy.

Vulvar Cancer

Authorization of 6 months may be granted for subsequent treatment of advanced or recurrent/ metastatic vulvar cancer when either of the following criteria is met:

- Disease is HPV-related and the requested medication will be used as a single agent.
- The requested medication will be used in combination with ipilimumab.

Gastric Cancer

Authorization of 6 months may be granted for treatment of gastric cancer in any of the following settings:

- When the requested medication will be used as first-line therapy in combination with chemotherapy for treatment of gastric adenocarcinoma for members who are not surgical candidates or have unresectable, recurrent, or metastatic disease that is HER2 negative and PD-L1 ≥ 1.
- When the requested medication will be used as a single agent, in combination with ipilimumab, or in combination with chemotherapy for treatment of gastric adenocarcinoma if tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).

Small Cell Lung Cancer

Authorization of 6 months may be granted for subsequent treatment of relapsed or progressive small cell lung cancer as a single agent.

Cervical Cancer

Authorization of 6 months may be granted for subsequent treatment of cervical cancer when one of the following criteria is met:

- The requested medication will be used as a single agent and member has recurrent or metastatic PD-L1 positive (combined positive score [CPS] ≥1) disease.
- The requested medication will be used in combination with ipilimumab and either of the following is met:
  - Disease is recurrent or metastatic.
  - Disease is persistent small cell neuroendocrine carcinoma of the cervix (NECC).

Pediatric Diffuse High-Grade Gliomas

Authorization of 6 months may be granted for hypermutant tumor pediatric diffuse high-grade glioma as adjuvant treatment or for recurrent or progressive disease.

Pediatric Primary Mediastinal Large B-Cell Lymphoma

Authorization of 6 months may be granted as a single agent or in combination with brentuximab vedotin for treatment of relapsed or refractory primary mediastinal large B-cell lymphoma.

Kaposi Sarcoma

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for subsequent treatment of relapsed/refractory advanced Kaposi Sarcoma.

Bone Cancer

Authorization of 6 months may be granted in combination with ipilimumab for unresectable or metastatic chondrosarcoma, chordoma, Ewing sarcoma, or osteosarcoma when all of the following criteria are met:

- Disease has tumor mutational burden-high (TMB-H) [≥10 mut/Mb] tumors.
- Disease has progressed following prior treatment and has no satisfactory alternative treatment options.

Authorization of 6 months may be granted as a single agent or in combination with sunitinib for dedifferentiated chondrosarcoma.

Biliary Tract Cancers (Cholangiocarcinoma and Gallbladder Cancer)

Authorization of 6 months may be granted in combination with ipilimumab for subsequent treatment of unresectable, gross residual (R2), or metastatic extrahepatic or intrahepatic cholangiocarcinoma or gallbladder cancer that is tumor mutational burden-high (TMB-H).

Authorization of 6 months may be granted in combination with ipilimumab for neoadjuvant treatment of resectable locoregionally advanced gallbladder cancer that is tumor mutational burden-high (TMB-H) when disease does not present as jaundice.

Soft Tissue Sarcoma

Authorization of 6 months may be granted for treatment of soft tissue sarcoma in the following settings:

- The requested medication will be used as a single agent or in combination with ipilimumab for treatment of extremity/body wall sarcomas, head/neck sarcomas, retroperitoneal/intra-abdominal sarcomas, and dedifferentiated liposarcoma.
- The requested medication will be used as a single agent or in combination with ipilimumab for treatment of rhabdomyosarcoma and epithelioid hemangioendothelioma that is tumor mutational burden-high (TMB-H) [≥10 mut/Mb].
- The requested medication will be used in combination with ipilimumab for the treatment of angiosarcoma.

Anaplastic Thyroid Carcinoma

Authorization of 6 months may be granted as a single agent for treatment of stage IVC anaplastic thyroid carcinoma.

Histologic (Richter) Transformation to Diffuse Large B-cell Lymphoma

Authorization of 6 months may be granted for treatment of Histologic (Richter) transformation to diffuse large B-cell lymphoma as a single agent or in combination ibrutinib.

Vaginal Cancer

Authorization of 6 months may be granted as subsequent therapy for recurrent or metastatic vaginal cancer when the requested medication will be used as a single agent or in combination with ipilimumab.

Squamous Cell Skin Carcinoma

Authorization of 6 months may be granted as a single agent for treatment of squamous cell skin carcinoma and either of the following is met:

- Disease is locally advanced, recurrent, unresectable, inoperable, or incompletely resected that is not curable by surgery or radiation.
- Disease is metastatic.

Adrenal Gland Tumors

Authorization of 6 months may be granted in combination with ipilimumab for treatment of unresectable or metastatic adrenocortical carcinoma.

CONTINUATION OF THERAPY

Adjuvant Treatment of Melanoma

Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for cutaneous melanoma who have not experienced disease recurrence or an unacceptable toxicity.

Urothelial Carcinoma

Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for adjuvant treatment of urothelial carcinoma who have not experienced disease recurrence or an unacceptable toxicity.

Authorization of 6 months may be granted (up to 24 months total) for continued treatment in members requesting reauthorization for urothelial carcinoma when the requested medication is used in combination with gemcitabine and cisplatin for up to 6 cycles followed by nivolumab maintenance therapy when the member has not experienced disease progression or an unacceptable toxicity.

Non-Small Cell Lung Cancer, Pleural or Peritoneal Mesothelioma

Authorization of 6 months may be granted (up to 24 months total when used in combination with ipilimumab) for continued treatment in members requesting reauthorization for non-small cell lung cancer (NSCLC) or pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma subtypes, when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Authorization of 3 months of therapy total (up to 3 cycles total) may be granted for neoadjuvant treatment of resectable NSCLC when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Authorization of 6 months may be granted for neoadjuvant treatment of resectable NSCLC (up to 4 cycles in combination with chemotherapy, followed by single agent adjuvant treatment up to 13 cycles) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Renal Cell Carcinoma

Authorization of 6 months may be granted (up to 24 months total when used in combination with cabozantinib) for continued treatment in members requesting reauthorization for renal cell carcinoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Gastric Cancer, Esophageal Cancer, and Esophagogastric Junction Carcinoma

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for gastric cancer, esophageal cancer, and esophagogastric junction carcinoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen for the following durations of therapy:

- Esophageal squamous cell carcinoma in combination with ipilimumab or chemotherapy for up to 24 months
- Unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma as a single agent until disease progression or unacceptable toxicity

- Adjuvant treatment of resected esophageal or esophagogastric junction cancer as a single agent for up to 12 months
- Gastric cancer, esophagogastric junction cancer, and esophageal adenocarcinoma in combination with chemotherapy for up to 24 months
- Gastric cancer in members who have completed endoscopic resection for up to 24 months

Biliary Tract Cancer

Authorization of 6 months may be granted (for 2 to 6 months total for neoadjuvant treatment, and for up 24 months total for other clinical settings) for continued treatment in members requesting reauthorization for biliary tract cancer when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Squamous Cell Skin Carcinoma

Authorization of 6 months may be granted (up to 24 months total) for continued treatment in members requesting reauthorization for squamous cell skin carcinoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

All Other Indications

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for all other indications listed in the Coverage Criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Opdivo (Nivolumab)	Ampullary Adenocarcinoma	Route of Administration: Intravenous 240 mg every 2 weeks 480 mg every 4 weeks Initial: 3mg/kg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks or 480 mg every 4 weeks
Opdivo (Nivolumab)	Anal Carcinoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks
Opdivo (Nivolumab)	Anaplastic Thyroid Carcinoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks
Opdivo (Nivolumab)	Biliary Tract Cancer: Gallbladder Cancer, Cholangiocarcinoma	Route of Administration: Intravenous 240mg every 2 weeks
Opdivo (Nivolumab)	Bone Cancer	Route of Administration: Intravenous 240mg every 2 weeks
Opdivo (Nivolumab)	Cervical Cancer	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 1mg/kg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks

Opdivo (Nivolumab)	Classical Hodgkin Lymphoma	Route of Administration: Intravenous ≥12 year(s) ≥40kg 240mg every 2 weeks for 6 doses ≥12 year(s) <40kg 3mg/kg every 2 weeks for 6 doses ≥18 year(s) 240mg every 2 weeks 480mg every 4 weeks 3mg/kg every 3 weeks for 4 to 8 doses
Opdivo (Nivolumab)	CNS Cancer: Brain Metastases	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 1mg/kg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks or 480 mg every 4 weeks
Opdivo(Nivolumab)	Colorectal Cancer, including Appendiceal Adenocarcinoma and Anal Adenocarcinoma	Route of Administration: Intravenous ≥12 year(s) ≥40kg 240mg every 2 weeks 480mg every 4 weeks Initial: 240mg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks or 480mg every 4 weeks Initial: 3mg/kg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks or 480 mg every 4 weeks ≥12 year(s) <40kg 3mg/kg every 2 weeks 6mg/kg every 4 weeks Initial: 3mg/kg every 3 weeks for 4 doses Maintenance: 3mg/kg every 2 weeks or 6mg/kg every 4 weeks
Opdivo (Nivolumab)	Endometrial Carcinoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 3mg/kg every 2 weeks for 8 doses Maintenance: 480mg every 4 weeks
Opdivo (Nivolumab)	Esophageal Cancer, Gastroesophageal Junction Cancer	Route of Administration: Intravenous 480mg every 4 weeks
Opdivo (Nivolumab)	Esophageal Cancer, Gastroesophageal Junction Cancer, Gastric Cancer	Route of Administration: Intravenous 240mg every 2 weeks 360mg every 3 weeks

Opdivo (Nivolumab)	Extranodal NK/T-Cell Lymphomas	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks
Opdivo (Nivolumab)	Gestational Trophoblastic Neoplasia	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks
Opdivo (Nivolumab)	Head and Neck Cancer, Squamous Cell Carcinoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks
Opdivo (Nivolumab)	Hepatocellular Carcinoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 1mg/kg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks or 480 mg every 4 weeks
Opdivo(Nivolumab)	Histologic (Richter) Transformation to Diffuse Large B-cell Lymphoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks
Opdivo (Nivolumab)	Kaposi Sarcoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks
Opdivo (Nivolumab)	Melanoma	Route of Administration: Intravenous ≥40kg Initial: 3mg/kg every 3 weeks for 4 doses Maintenance: 480mg every 4 weeks beginning 6 weeks after initial dose Initial: 240mg every 3 weeks for 2 doses, followed by therapeutic lymph node dissection (TLND) (Neoadjuvant) Maintenance: 480 mg every 4 weeks beginning 6-12 weeks after TLND (Adjuvant) <u>≥12 year(s)</u> <40kg 3mg/kg every 2 weeks 6mg/kg every 4 weeks Initial: 1mg/kg every 3 weeks for 4 doses Maintenance: 3mg/kg every 2 weeks or 6 mg/kg every 4 weeks
Opdivo (Nivolumab)	Melanoma or Uveal Melanoma	Route of Administration: Intravenous <u>≥12 year(s)</u> ≥40kg 240mg every 2 weeks 480mg every 4 weeks Initial: 1mg/kg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks or 480 mg every 4 weeks
Opdivo (Nivolumab)	Merkel Cell Carcinoma	Route of Administration: Intravenous 240mg every 2 weeks Initial: 3mg/kg every 3 weeks for 4 doses Maintenance: 3mg/kg every 2 weeks
Opdivo (Nivolumab)	Merkel Cell Carcinoma, Neoadjuvant	Route of Administration: Intravenous 240mg every 2 weeks for 2 doses

Opdivo (Nivolumab)	Mesothelioma (Pleural, Peritoneal, Pericardial, or Tunica Vaginalis Testis)	Route of Administration: Intravenous 240mg every 2 weeks 360mg every 3 weeks 480mg every 4 weeks
Opdivo (Nivolumab)	Non-Small Cell Lung Cancer (NSCLC)	Route of Administration: Intravenous 360mg every 3 weeks
Opdivo (Nivolumab)	Non-Small Cell Lung Cancer or Small Cell Lung Cancer	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks
Opdivo (Nivolumab)	Non-Small Cell Lung Cancer, Neoadjuvant	Route of Administration: Intravenous 360mg every 3 weeks for 3 doses
Opdivo (Nivolumab)	Non-Small Cell Lung Cancer, Neoadjuvant and Adjuvant	Route of Administration: Intravenous Initial: 360mg every 3 weeks for 4 doses (neoadjuvant) Maintenance: 480mg every 4 weeks as adjuvant treatment after surgery
Opdivo (Nivolumab)	Pediatric Diffuse High-Grade Gliomas	Route of Administration: Intravenous <18year(s) 3mg/kg every 2 weeks
Opdivo (Nivolumab)	Pediatric Primary Mediastinal Large B-Cell Lymphoma	Route of Administration: Intravenous <18year(s) 3mg/kg every 2 weeks
Opdivo (Nivolumab)	Renal Cell Carcinoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 3mg/kg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks or 480mg every 4 weeks
Opdivo (Nivolumab)	Small Bowel Adenocarcinoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 3mg/kg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks
Opdivo (Nivolumab)	Soft Tissue Sarcoma: Angiosarcoma, Extremity/Body Wall Sarcoma, Head/Neck Sarcoma, Retroperitoneal/Intra-Abdominal Sarcoma, Rhabdomyosarcoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 3mg/kg every 3 weeks for 4 doses Maintenance: 3mg/kg every 2 weeks
Opdivo (Nivolumab)	Squamous Cell Skin Cancer	Route of Administration: Intravenous 240mg every 2 weeks 3mg/kg every 2 weeks
Opdivo (Nivolumab)	Urothelial Carcinoma	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 360mg every 3 weeks for 6 doses Maintenance: 480mg every 4 weeks

Opdivo (Nivolumab)	Vaginal Cancer	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 1mg/kg every 3 weeks for 4 doses Maintenance: 240 mg every 2 weeks
Opdivo (Nivolumab)	Vulvar Cancer	Route of Administration: Intravenous 240mg every 2 weeks 480mg every 4 weeks Initial: 1mg/kg every 3 weeks for 4 doses Maintenance: 240mg every 2 weeks

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.

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).

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EFFECTIVE DATE 10/31/26

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