Reference number(s)
2345-A

Standard Medicare Part B Management Opdivo

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over the counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Opdivo	nivolumab

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[1]

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 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.

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- 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.

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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 Cancer

- 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, and 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[2]

- Cutaneous melanoma
- Non-small cell lung cancer
- Colorectal cancer, including anal adenocarcinoma
- Appendiceal neoplasms and cancers
- Urothelial carcinoma
    - Bladder cancer

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    - Primary carcinoma of the urethra
    - Upper genitourinary tract tumors
    - Urothelial carcinoma of the prostate
- Renal cell carcinoma
- Head and neck cancers
    - Very advanced head and neck cancer
    - Mucosal melanoma
    - Cancer of the nasopharynx
- Classic Hodgkin lymphoma
- Hepatocellular carcinoma
- Uveal melanoma
- Anal carcinoma
- Merkel cell carcinoma
- Central nervous system (CNS) brain metastases
- Pleural mesothelioma
- Peritoneal mesothelioma
- Gestational trophoblastic neoplasia
- Diffuse large B-cell lymphoma
    - Primary mediastinal large B-cell lymphoma
    - Histologic (Richter's) transformation to diffuse large B-cell lymphoma
- Esophageal and esophagogastric junction cancers
- Small bowel adenocarcinoma
- Ampullary adenocarcinoma
- Extranodal NK/T-cell lymphoma
- Neuroendocrine and adrenal tumors
    - Poorly differentiated neuroendocrine carcinoma/large or small cell carcinoma
    - Well-differentiated grade 3 neuroendocrine tumors
    - Adrenal gland tumors
- Uterine Neoplasms
    - Endometrial Carcinoma
    - Uterine Sarcoma
- Vulvar cancer
- Gastric cancer
- Biliary tract cancers
    - Gallbladder cancer
    - Intrahepatic cholangiocarcinoma
    - Extrahepatic cholangiocarcinoma
- Cervical cancer
- Small cell lung cancer
- Kaposi Sarcoma
- Bone Cancer
- Pediatric Diffuse High-Grade Gliomas
- Soft Tissue Sarcoma
    - Extremity/body wall sarcoma
    - Head/neck sarcoma
    - Retroperitoneal/intra-abdominal sarcoma

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    - Rhabdomyosarcoma
    - Angiosarcoma
    - Dedifferentiated liposarcoma
    - Epithelioid hemangioendothelioma
- Pancreatic adenocarcinoma
- Anaplastic thyroid carcinoma
- Vaginal cancer
- Squamous Cell Skin Carcinoma

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following documentation must be available, upon request, for all submissions:

- 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 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[1,2]

Authorization of 12 months may be granted for treatment of cutaneous melanoma when any of the following apply:

- The requested medication will be used for treatment of unresectable or metastatic disease.

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- The requested medication will be used 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 complete resection.
- The requested medication will be used as neoadjuvant treatment of resectable disease.

Non-Small Cell Lung Cancer[1,2,4]

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC when both of the following conditions 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.

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 L858 mutations, or ALK, RET, or ROS1 gene fusions (unless testing is not feasible due to insufficient tissue).

Authorization of 12 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).

Colorectal Cancer[1-3]

Authorization of 12 months may be granted for treatment of colorectal cancer, including anal adenocarcinoma, when member has 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).

Appendiceal Neoplasms and Cancers[2,5]

Authorization of 12 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 Opdivo as a single agent).

Urothelial Carcinoma[1,2]

Authorization of 12 months may be granted for treatment of urothelial carcinoma, including bladder cancer, upper genitourinary tract tumors, urothelial carcinoma of the prostate, and primary carcinoma of the urethra.

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Renal Cell Carcinoma[1,2]

Authorization of 12 months may be granted for treatment of renal cell carcinoma for relapsed, advanced, or stage IV disease.

Head and Neck Cancers[1,2]

Authorization of 12 months may be granted for treatment of head and neck cancers, including very advanced head and neck cancer, mucosal melanoma, and cancer of the nasopharynx.

Classic Hodgkin Lymphoma (cHL)[1,2]

Authorization of 12 months may be granted for the treatment of classic Hodgkin lymphoma.

Hepatocellular Carcinoma[1,2]

Authorization of 12 months may be granted for treatment of hepatocellular carcinoma.

Uveal Melanoma[2]

Authorization of 12 months may be granted for treatment of uveal melanoma.

Anal Carcinoma[2]

Authorization of 12 months may be granted for treatment of anal carcinoma.

Merkel Cell Carcinoma[2]

Authorization of 12 months may be granted for treatment of Merkel cell carcinoma.

CNS Brain Metastases[2]

Authorization of 12 months may be granted for treatment of CNS brain metastases in patients with melanoma (including leptomeningeal metastases) or NSCLC.

Pleural or Peritoneal Mesothelioma[2]

Authorization of 12 months may be granted for 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.

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Gestational Trophoblastic Neoplasia[2]

Authorization of 12 months may be granted for treatment of gestational trophoblastic neoplasia.

Diffuse Large B-Cell Lymphoma[2]

Authorization of 12 months may be granted for treatment of either of the following:

- Primary mediastinal large B-cell lymphoma.
- Histologic (Richter's) transformation to diffuse large B-cell lymphoma.

Esophageal and Esophagogastric Junction Cancer[1,2]

Authorization of 12 months may be granted for treatment of esophageal and 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 ≥ 1in combination with ipilimumab or chemotherapy.
- Subsequent therapy.

Authorization of 12 months may be granted for adjuvant treatment of completely resected esophageal or esophagogastric junction cancer with residual pathologic disease.

Authorization of 12 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 12 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.

Small Bowel Adenocarcinoma[2]

Authorization of 12 months may be granted 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), as a single agent or in combination with ipilimumab.

Ampullary Adenocarcinoma[2]

Authorization of 12 months may be granted for treatment of progressive or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) ampullary adenocarcinoma in combination with ipilimumab.

Extranodal NK/T-Cell Lymphoma[2]

Authorization of 12 months may be granted for treatment of extranodal NK/T-cell lymphoma.

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Neuroendocrine and Adrenal Tumors[2]

Authorization of 12 months may be granted for subsequent treatment of metastatic extrapulmonary poorly differentiated neuroendocrine carcinoma/large or small cell carcinoma/mixed neuroendocrine-non-neuroendocrine neoplasm in combination with ipilimumab.

Authorization of 12 months may be granted for treatment of locally advanced/metastatic well-differentiated grade 3 neuroendocrine tumors with unfavorable biology (e.g., relatively high Ki-67 [≥55%], rapid growth rate, negative somatostatin receptor (SSTR)-based positron emission tomography (PET) imaging) in combination with ipilimumab.

Authorization of 12 months may be granted in combination with ipilimumab for treatment of unresectable or metastatic adrenocortical carcinoma.

Uterine Neoplasms[2]

Authorization of 12 months may be granted as a single agent for subsequent treatment of recurrent unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) endometrial carcinoma.

Authorization of 12 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 12 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.

Vulvar Cancer[2]

Authorization of 12 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[2]

Authorization of 12 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).

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Biliary Tract Cancers[2]

Authorization of 12 months may be granted for treatment of biliary tract cancers, including gallbladder cancer, intrahepatic cholangiocarcinoma, and extrahepatic cholangiocarcinoma.

Cervical Cancer[2]

Authorization of 12 months may be granted for subsequent treatment of recurrent or metastatic cervical cancer or recurrent, metastatic, or persistent small cell neuroendocrine carcinoma of the cervix (NECC).

Small Cell Lung Cancer[2]

Authorization of 12 months may be granted for subsequent treatment of relapsed or progressive small cell lung cancer.

Kaposi Sarcoma[2]

Authorization of 12 months may be granted as a single agent or in combination with ipilimumab for subsequent treatment of relapsed/refractory advanced Kaposi Sarcoma.

Bone Cancer[2]

Authorization of 12 months may be granted in combination with ipilimumab for unresectable or metastatic bone cancer with tumor mutational burden-high (TMB-H) [≥10 mut/Mb] tumors.

Authorization of 12 months may be granted as a single agent or in combination with sunitinib for dedifferentiated chondrosarcoma.

Pediatric Diffuse High-Grade Gliomas[2]

Authorization of 12 months may be granted for hypermutant tumor pediatric diffuse high-grade glioma as adjuvant treatment or for recurrent or progressive disease.

Soft Tissue Sarcoma[2]

Authorization of 12 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, rhabdomyosarcoma, dedifferentiated liposarcoma, and epithelioid hemangioendothelioma.
- The requested medication will be used in combination with ipilimumab for the treatment of angiosarcoma.

Pancreatic Adenocarcinoma[2]

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Authorization of 12 months may be granted in combination with ipilimumab for treatment of locally advanced, metastatic, or recurrent pancreatic adenocarcinoma with tumor mutational burden-high (TMB-H) [≥10 mut/Mb] tumors.

Anaplastic Thyroid Carcinoma[2]

Authorization of 12 months may be granted as a single agent for treatment of stage IVC anaplastic thyroid carcinoma.

Vaginal Cancer[2]

Authorization of 12 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[2]

Authorization of 12 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.

Continuation of Therapy

Adjuvant Treatment of Melanoma

Authorization for 12 months total therapy may be granted for all members (including new members) who are continuing with the requested therapy when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used as adjuvant treatment for a member with melanoma.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease recurrence while on the current regimen.

Non-Small Cell Lung Cancer, Pleural or Peritoneal Mesothelioma

Authorization for 12 months may be granted for all members (including new members) who are continuing with the requested therapy when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease progression while on the current regimen.

Therapy durations will be limited to the following:

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- Non-small cell lung cancer or pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma subtypes, will be approved for up to 24 months when used in combination with ipilimumab.
- Neoadjuvant treatment of resectable NSCLC will be approved for a total of 3 months of therapy (up to 3 cycles).
- Authorization of 12 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).

Urothelial Carcinoma

Authorization for up to 12 months total may be granted for continued adjuvant treatment of urothelial carcinoma in all members (including new members) who are continuing with the requested therapy when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat urothelial carcinoma.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease progression while on the current regimen.

Authorization for 12 months may be granted (up to 24 months total) when used in combination with gemcitabine and cisplatin for up to 6 cycles followed by nivolumab maintenance therapy for all members (including new members) who are continuing with the requested therapy when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat urothelial carcinoma.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease progression while on the current regimen.

Renal Cell Carcinoma

Authorization for 12 months may be granted (up to 24 months total when used in combination with cabozantinib) for all members (including new members) who are continuing with the requested therapy when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat renal cell carcinoma.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease progression while on the current regimen.

Gastric Cancer, Esophageal Cancer, and Esophagogastric Junction Carcinoma

Authorization of 12 months may be granted for all members (including new members) who are continuing with the requested therapy when all of the following criteria are met:

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- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease progression while on the current regimen.

Therapy durations will be limited to the following:

- 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 for 12 months may be granted (for 2 to 6 months total for neoadjuvant treatment, and for up 24 months total for other clinical settings) for all members (including new members) who are continuing with the requested therapy when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat biliary tract cancer.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease progression while on the current regimen.

Squamous Cell Skin Carcinoma

Authorization for 12 months may be granted (up to 24 months total) for all members (including new members) who are continuing with the requested therapy when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat squamous cell skin carcinoma.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease progression while on the current regimen.

All Other Indications

Authorization for 12 months may be granted for all members (including new members) who are continuing with the requested therapy when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat any other diagnosis or condition listed in the coverage criteria section.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND

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- No evidence of disease progression while on the current regimen.

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Opdivo.
- The available compendium
  - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
  - Micromedex DrugDex
  - American Hospital Formulary Service- Drug Information (AHFS-DI)
  - Lexi-Drugs
  - Clinical Pharmacology
- NCCN Guideline: Hodgkin lymphoma
- NCCN Guideline: Small cell lung cancer
- NCCN Guideline: Vulvar cancer
- NCCN Guideline: Cervical cancer
- NCCN Guideline: Gestational trophoblastic neoplasia
- NCCN Guideline: Small bowel adenocarcinoma
- NCCN Guideline: Peritoneal mesothelioma
- NCCN Guideline: Pleural mesothelioma
- NCCN Guideline: T-cell lymphomas
- NCCN Guideline: Pediatric Hodgkin lymphoma
- NCCN Guideline: Cutaneous melanoma
- NCCN Guideline: Merkel cell carcinoma
- NCCN Guideline: Non-small cell lung cancer
- NCCN Guideline: Hepatocellular carcinoma
- NCCN Guideline: Anal carcinoma
- NCCN Guideline: Uveal melanoma
- NCCN Guideline: Gastric cancer
- NCCN Guideline: Esophageal and esophagogastric junction
- NCCN Guideline: Central nervous system cancers
- NCCN Guideline: Biliary tract cancers
- NCCN Guideline: Ampullary adenocarcinoma
- NCCN Guideline: Bladder cancer
- NCCN Guideline: Colon cancer
- NCCN Guideline: Rectal cancer
- NCCN Guideline: Head and neck cancers
- NCCN Guideline: Kidney cancer
- NCCN Guideline: Pediatric central nervous system cancers
- NCCN Guideline: Pancreatic adenocarcinoma
- NCCN Guideline: Chronic lymphocytic leukemia/Small lymphocytic lymphoma
- NCCN Guideline: Pediatric aggressive mature b-cell lymphomas
- NCCN Guideline: Soft Tissue Sarcoma
- NCCN Guideline: Neuroendocrine and Adrenal Tumors

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- NCCN Guideline: Uterine Neoplasms
- NCCN Guideline: B-cell Lymphomas
- NCCN Guideline: Thyroid carcinoma
- NCCN Guideline: Vaginal cancer
- NCCN Guideline: Squamous cell skin cancer
- NCCN Guideline: Appendiceal neoplasms and cancers

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Opdivo and are included in addition to the following:

- Cutaneous melanoma
- Non-small cell lung cancer
- Colorectal cancer, including anal adenocarcinoma
- Appendiceal neoplasms and cancers
- Urothelial carcinoma
- Renal cell carcinoma
- Head and neck cancers
- Classic Hodgkin lymphoma
- Hepatocellular carcinoma
- Uveal melanoma
- Anal carcinoma
- Merkel cell carcinoma
- Central nervous system (CNS) brain metastases
- Pleural mesothelioma
- Peritoneal mesothelioma
- Gestational trophoblastic neoplasia
- Diffuse large B-cell lymphoma
- Small bowel adenocarcinoma
- Ampullary adenocarcinoma
- Extranodal natural killer (NK)/T-cell lymphoma
- Neuroendocrine and adrenal tumors
- Uterine neoplasms
- Vulvar carcinoma
- Gastric cancer
- Esophageal and esophagogastric junction cancers
- Biliary tract cancers
- Cervical cancer
- Small cell lung cancer
- Kaposi sarcoma
- Bone cancer
- Pediatric diffuse high-grade gliomas
- Biliary tract cancers
- Soft tissue sarcoma
- Pancreatic adenocarcinoma
- Anaplastic thyroid carcinoma
- Vaginal cancer
- Squamous skin cell carcinoma

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Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Opdivo to treat the indications in coverage criteria section can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

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