Reference number(s)
1980-A

Standard Medicare Part B Management Keytruda

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
Keytruda	pembrolizumab

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]

Melanoma

- Keytruda (pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma.
- Keytruda is indicated for the adjuvant treatment of adult and pediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma.

Non-Small Cell Lung Cancer

- Keytruda, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.
- Keytruda, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

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- Keytruda, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 (Tumor Proportion Score [TPS ≥1%]) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
    - stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
    - metastatic.
- Keytruda, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.
- Keytruda, in combination with platinum-containing chemotherapy, is indicated for the treatment of patients with resectable (tumors ≥4 cm or node positive) NSCLC as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.
- Keytruda, as a single agent, is indicated for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with stage 1B (T2a ≥ 4cm), II, or IIIA NSCLC

Malignant Pleural Mesothelioma

Keytruda, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic malignant pleural mesothelioma (MPM).

Head and Neck Cancer Squamous Cell Cancer

- Keytruda is indicated for the treatment of adult patients with resectable locally advanced HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, as a single agent as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without cisplatin and then as a single agent.
- Keytruda, in combination with platinum and fluorouracil (FU), is indicated for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC).
- Keytruda, as a single agent, is indicated for the first line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test.
- Keytruda, as a single agent, is indicated for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

Classical Hodgkin Lymphoma

- Keytruda is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL).
- Keytruda is indicated for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more prior lines of therapy.

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Primary Mediastinal Large B-cell Lymphoma

Keytruda is indicated for the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphomas (PMBCL), or who have relapsed after 2 or more prior lines of therapy.

Limitations of Use

Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

Urothelial Carcinoma

- Keytruda, as a single agent, is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma:
  - who are not eligible for any platinum-containing chemotherapy, or
  - who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
- Keytruda, as a single agent, is indicated for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.
- Keytruda, in combination with enfortumab vedotin, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer.

Microsatellite Instability-High or Mismatch Repair Deficient Cancer

Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer

Keytruda is indicated for the treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC) as determined by an FDA-approved test.

Gastric Cancer

- Keytruda is indicated in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS≥1) as determined by an FDA-approved test.
- Keytruda, in combination with fluoropyrimidine- and platinum-containing chemotherapy is indicated for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.

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Esophageal Cancer

Keytruda is indicated for the treatment of patients with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either:

- In combination with platinum- and fluoropyrimidine-based chemotherapy for patients with tumors that express PD-L1 (CPS ≥ 1), or
- As a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology whose tumors express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test.

Cervical Cancer

- Keytruda is indicated in combination with chemotherapy, with or without bevacizumab, for the treatment of patients with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.
- Keytruda is indicated as a single agent for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumor express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
- Keytruda, in combination with chemoradiotherapy (CRT), is indicated for the treatment of patients with FIGO 2014 Stage III-IVA cervical cancer.

Hepatocellular Carcinoma

Keytruda is indicated for the treatment of patients with hepatocellular carcinoma (HCC) secondary to hepatitis B who have received prior systemic therapy other than a PD-1/PD-L1- containing regimen.

Biliary Tract Cancer

Keytruda, in combination with gemcitabine and cisplatin is indicated for the treatment of patients with locally advanced unresectable or metastatic biliary tract cancer (BTC).

Merkel Cell Carcinoma

Keytruda is indicated for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC).

Renal Cell Carcinoma

- Keytruda, in combination with axitinib, is indicated for the first-line treatment of adult patients with advanced renal cell carcinoma (RCC).
- Keytruda, in combination with lenvatinib, is indicated for the first-line treatment of adult patients with advanced RCC.
- Keytruda, is indicated for the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

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Endometrial Carcinoma

- Keytruda, in combination with carboplatin and paclitaxel, followed by Keytruda as a single agent, for the treatment of adult patients with primary advanced or recurrent endometrial carcinoma.
- Keytruda, in combination with lenvatinib, is indicated for the treatment of adult patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) or not MSI-H as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.
- Keytruda, as a single agent, is indicated for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

Tumor Mutational Burden-High Cancer

Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

Limitations of use

The safety and effectiveness of Keytruda in pediatric patients with TMB-H central nervous system cancers have not been established.

Cutaneous Squamous Cell Carcinoma

Keytruda is indicated for the treatment of patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC that is not curable by surgery or radiation.

Triple-Negative Breast Cancer

- Keytruda is indicated for the treatment of patients with high-risk early-stage triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.
- Keytruda is indicated in combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA approved test.

Adult Classical Hodgkin Lymphoma and Adult Primary Mediastinal Large B-Cell Lymphoma

Additional Dosing Regimen of 400mg Every 6 Weeks.

Keytruda is indicated for use at an additional recommended dosage of 400mg every 6 weeks for classical Hodgkin lymphoma and primary mediastinal large B-cell lymphoma in adults.

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Compendial Uses[2]

- Cutaneous melanoma
- Non-small cell lung cancer
- Head and neck cancer
- Classical Hodgkin lymphoma
- Urothelial carcinoma
- Anaplastic thyroid carcinoma
- Follicular, Oncocytic (Hurthle cell), or papillary thyroid carcinoma
- Colorectal cancer
- Merkel cell carcinoma
- Gastric cancer
- Esophageal cancer and esophagogastric junction cancer
- Cervical cancer
- Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
- Uveal melanoma
- Testicular cancer
- Endometrial carcinoma
- Anal carcinoma
- Central Nervous System (CNS) brain metastases
- Primary mediastinal large B-cell lymphoma
- Pancreatic adenocarcinoma
- Biliary Tract cancers
- Hepatocellular carcinoma
- Vulvar cancer
- Renal cell carcinoma
- Thymic carcinoma
- Mycosis Fungoides/Sezary syndrome
- Anaplastic large cell lymphoma (ALCL)
- Extranodal NK/T-cell lymphoma
- Gestational trophoblastic neoplasia
- Neuroendocrine and Adrenal Tumors
- Prostate cancer
- Cutaneous squamous cell skin cancer
- Occult primary cancer
- Small bowel adenocarcinoma
- Breast cancer
- Bone cancer
- Histologic (Richter) transformation to diffuse large B-cell lymphoma
- Penile cancer
- Soft tissue sarcoma
- Uterine sarcoma

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- Ampullary Adenocarcinoma
- Small cell lung cancer
- Pediatric Diffuse High-Grade Gliomas
- Kaposi Sarcoma
- Vaginal Cancer
- Pleural or Peritoneal mesothelioma

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this document 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 laboratory report confirming high tumor mutational burden (≥10 mutations/megabase [mut/Mb]), where applicable.
- Documentation of laboratory report confirming that the cancer cells are negative for the following receptors, where applicable:
    - Human epidermal growth factor receptor 2 (HER-2)
    - Estrogen
    - Progesterone

Exclusions

Coverage will not be provided for members with any of the following exclusions:

- Pediatric members with TMB-H central nervous system cancers.
- Members who have experienced disease progression while on programmed death receptor-1 (PD-1) or PD-L1 inhibitor therapy (other than when used as subsequent therapy for metastatic or unresectable melanoma in combination with ipilimumab or lenvatinib).

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Coverage Criteria

Cutaneous Melanoma[1,2]

Authorization of 12 months may be granted for the treatment of cutaneous melanoma in any of the following settings:

- Unresectable disease
- Metastatic disease
- Adjuvant treatment
- Neoadjuvant treatment

Non-small Cell Lung Cancer (NSCLC)[1,2]

Authorization of 12 months may be granted for NSCLC for any of the following clinical settings:

- Treatment of recurrent, advanced, or metastatic disease.
- Neoadjuvant treatment when used in combination with platinum-based chemotherapy, and then continued as single agent adjuvant therapy after surgery.
- Adjuvant treatment following resection and platinum-based chemotherapy.

Head and Neck Cancer[1,2]

Authorization of 12 months may be granted for treatment of head and neck cancer.

Classic Hodgkin Lymphoma (cHL)[1,2]

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

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.

Solid Tumors[1,2]

Authorization of 12 months may be granted for treatment of solid tumors in members with unresectable or metastatic disease that has progressed following prior treatment and have no satisfactory alternative treatment options when either of the following criteria is met:

- The requested medication will be used for microsatellite instability-high or mismatch repair deficient solid tumors.

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- The requested medication will be used for tumor mutational burden-high (≥10 mutations/megabase) solid tumors.

Neuroendocrine and Adrenal Tumors[2]

Authorization of 12 months may be granted for treatment of neuroendocrine and adrenal tumors.

Anaplastic Thyroid Carcinoma[2]

Authorization of 12 months may be granted for treatment of anaplastic thyroid carcinoma for tumor mutational burden-high (≥10 mutations/megabase) tumors or stage IVC disease.

Follicular, Oncocytic (Hurthle Cell), or Papillary Thyroid Carcinoma[2]

Authorization of 12 months may be granted for treatment of follicular, oncocytic (Hurthle cell), or papillary thyroid carcinoma when any of the following criteria are met:

- Disease is microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR) or tumor mutational burden-high (≥10 mutations/megabase)
- The member experienced disease progression on single agent lenvatinib and the requested medication will be used in combination with lenvatinib

Colorectal Cancer (CRC)[1,2]

Authorization of 12 months may be granted for treatment of colorectal cancer including appendiceal carcinoma for microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or polymerase epsilon/delta (POLE/POLD1) tumors with ultra-hypermutated phenotype (TMB > 50 mut/Mb).

Merkel Cell Carcinoma (MCC)[1]

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

Gastric Cancer[1,2]

Authorization of 12 months may be granted for treatment of gastric cancer.

Esophageal Cancer and Esophagogastric Junction Cancer[1,2]

Authorization of 12 months may be granted for treatment of esophageal cancer, including esophagogastric junction (EGJ) cancer.

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Cervical Cancer[1,2]

Authorization of 12 months may be granted for treatment of cervical cancer.

Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer[2]

Authorization of 12 months may be granted for the treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

Uveal Melanoma[2]

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

Testicular Cancer[2]

Authorization of 12 months may be granted for the treatment of testicular cancer.

Endometrial Carcinoma[1,2]

Authorization of 12 months may be granted for the treatment of endometrial carcinoma.

Anal Carcinoma[2]

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

CNS Brain Metastases[2]

Authorization of 12 months may be granted for the treatment of CNS brain metastases.

Primary Mediastinal Large B-Cell Lymphoma (PMBCL)[1,2]

Authorization of 12 months may be granted for the treatment of primary mediastinal large B-cell lymphoma.

Pancreatic Adenocarcinoma[2]

Authorization of 12 months may be granted for the treatment of pancreatic adenocarcinoma.

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Biliary Tract Cancers[1,2]

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

Hepatocellular Carcinoma (HCC)[1,2]

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

Vulvar Cancer[2]

Authorization of 12 months may be granted for treatment of vulvar cancer.

Renal Cell Carcinoma (RCC)[1,2]

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

Thymic Carcinoma[2]

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

Mycosis Fungoides/Sezary Syndrome[2]

Authorization of 12 months may be granted for treatment of mycosis fungoides or Sezary syndrome.

Extranodal NK/T-cell lymphoma[2]

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

Anaplastic large cell lymphoma (ALCL)[2]

Authorization of 12 months may be granted for treatment of anaplastic large cell lymphoma (ALCL).

Gestational Trophoblastic Neoplasia[2]

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

Prostate Cancer[2]

Authorization of 12 months may be granted for treatment of prostate cancer.

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Cutaneous Squamous Cell Skin Carcinoma (cSCC)[1]

Authorization of 12 months may be granted for treatment of cutaneous squamous cell carcinoma (cSCC) that is not curable by surgery or radiation.

Occult Primary[2]

Authorization of 12 months may be granted for treatment of occult primary cancer in members with microsatellite instability-high or mismatch repair deficient tumors or tumor mutational burden-high (TMB-H) (≥10 mutations/megabase (mut/Mb) tumors).

Small Bowel Adenocarcinoma[2]

Authorization of 12 months may be granted for treatment of small bowel adenocarcinoma, when both of the following criteria are met:

- Disease is unresectable, medically inoperable, advanced or metastatic.
- Member has microsatellite-instability high (MSI-H), mismatch repair deficient (dMMR), or polymerase epsilon/delta (POLE/POLD1) tumors with ultra-hypermutated phenotype (TMB > 50 mut/Mb).

Ampullary Adenocarcinoma[2]

Authorization of 12 months may be granted as a single agent for microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or tumor mutational burden-high (TMB-H ≥ 10 mut/Mb) ampullary adenocarcinoma.

Breast Cancer[1,2]

Authorization of 12 months may be granted for treatment of locally advanced or high-risk triple-negative breast cancer (TNBC) when both of the following criteria are met:

- The diagnosis of triple-negative breast cancer is confirmed by the cancer cells testing negative for ALL of the following receptors:
  - Human epidermal growth factor receptor 2 (HER-2)
  - Estrogen
  - Progesterone
- The requested medication will be used as either:
  - Neoadjuvant treatment in combination with chemotherapy; or
  - Continued adjuvant treatment after surgery, as a single agent.

Authorization of 12 months may be granted for treatment in members with no response to preoperative systemic therapy or for recurrent unresectable or metastatic TNBC when all of the following criteria are met:

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- The diagnosis of triple-negative breast cancer is confirmed by the cancer cells testing negative for ALL of the following receptors:
  - Human epidermal growth factor receptor 2 (HER-2)
  - Estrogen
  - Progesterone
- Tumor must express PD-L1.
- The requested medication will be used as a single agent or in combination with chemotherapy.

Bone Cancer[2]

Authorization of 12 months may be granted for treatment of bone cancer, including chondrosarcoma, chordoma, Ewing Sarcoma, osteosarcoma, and high-grade undifferentiated pleomorphic sarcoma.

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma[2]

Authorization of 12 months may be granted for treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma.

Penile Cancer[2]

Authorization of 12 months may be granted for treatment of penile cancer.

Soft Tissue Sarcoma[2]

Authorization of 12 months may be granted for treatment of the following types of soft tissue sarcoma:

- Extremity/body wall sarcoma, head/neck sarcoma, retroperitoneal/intra-abdominal sarcoma, rhabdomyosarcoma, cutaneous angiosarcoma, or dedifferentiated liposarcoma, as a single agent
- Alveolar soft part sarcoma (ASPS), as a single agent or in combination with axitinib (Inlyta).

Uterine sarcoma[2]

Authorization of 12 months may be granted for treatment of uterine sarcoma for tumor mutational burden-high (≥10 mutations/megabase) tumors.

Small Cell Lung Cancer[2]

Authorization of 12 months may be granted for treatment of small cell lung cancer.

Pediatric Diffuse High-Grade Gliomas[2]

Authorization of 12 months may be granted for treatment of hypermutant tumor pediatric diffuse high-grade glioma.

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Kaposi Sarcoma[2]

Authorization of 12 months may be granted as a single agent for subsequent treatment of relapsed/refractory Kaposi Sarcoma.

Vaginal Cancer[2]

Authorization of 12 months may be granted for treatment of vaginal cancer.

Pleural or peritoneal Mesothelioma[1,2]

Authorization of 12 months may be granted for first-line treatment of unresectable advanced or metastatic pleural or peritoneal mesothelioma when used in combination with pemetrexed and platinum chemotherapy.

Histologic (Richter) transformation to diffuse large B-cell lymphoma[2]

Authorization of 12 months may be granted for treatment of Histologic (Richter) transformation to diffuse large B-cell lymphoma as a single agent or in combination with ibrutinib.

Continuation of Therapy

Adjuvant treatment of melanoma, high-risk early-stage TNBC, renal cell carcinoma, or NSCLC

Authorization for 12 months total therapy may be granted for all members (including new members) who are continuing with the requested medication 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 any of the following indications: melanoma, high-risk early-stage TNBC, renal cell carcinoma, or NSCLC.
- 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.

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NSCLC, head and neck cancer, cHL, PMBCL, MSI-H or dMMR Cancers, Gastric Cancer, Esophageal Cancer (including EGJ), Cervical Cancer, urothelial carcinoma, HCC, MCC, RCC, Endometrial carcinoma, cSCC, locally recurrent unresectable or metastatic TNBC, TMB-H Cancer, Biliary Tract Cancer, pleural or peritoneal mesothelioma, Histologic (Richter) transformation to diffuse large B-cell lymphoma, penile cancer

Authorization for 12 months (up to 24 months of continuous use) may be granted for all members (including new members) who are continuing with the requested medication 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 NSCLC, head and neck cancer, cHL, PMBCL, MSI-H or dMMR cancers, gastric cancer, esophageal cancer (including EGJ), urothelial carcinoma, cervical cancer, HCC, MCC, RCC, endometrial carcinoma, cSCC, locally recurrent unresectable or metastatic TNBC, TMB-H cancers, biliary tract cancers, pleural or peritoneal mesothelioma, Histologic (Richter) transformation to diffuse large B-cell lymphoma, and penile 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 recurrence 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 medication 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 enumerated 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
    - No evidence of disease recurrence while on the current regimen.

Summary of Evidence

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

- The prescribing information for Keytruda.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium

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  - Micromedex DrugDex
  - American Hospital Formulary Service- Drug Information (AHFS-DI)
  - Lexi-Drugs
- NCCN Guideline: Pediatric central nervous system cancers
- NCCN Guideline: Prostate cancer
- NCCN Guideline: Penile cancer
- NCCN Guideline: Hodgkin lymphoma
- NCCN Guideline: Thymomas and thymic carcinomas
- NCCN Guideline: Small cell lung cancer
- NCCN Guideline: Neuroendocrine and Adrenal Tumors
- NCCN Guideline: Vulvar cancer
- NCCN Guideline: Cervical cancer
- NCCN Guideline: Gestational Trophoblastic Neoplasia
- NCCN Guideline: Small bowel adenocarcinoma
- NCCN Guideline: T-cell lymphomas
- NCCN Guideline: Pediatric Hodgkin lymphoma
- NCCN Guideline: Squamous cell skin cancer
- NCCN Guideline: Cutaneous melanoma
- NCCN Guideline: Kaposi sarcoma
- NCCN Guideline: Pediatric aggressive mature B-cell lymphomas
- NCCN Guideline: Bone cancer
- NCCN Guideline: Testicular cancer
- NCCN guideline: Merkel cell carcinoma
- NCCN guideline: Non-small cell lung cancer
- NCCN guideline: Breast cancer
- NCCN guideline: Hepatocellular carcinoma
- NCCN guideline: Soft tissue sarcoma
- NCCN guideline: Anal carcinoma
- NCCN guideline: Uveal melanoma
- NCCN guideline: Gastric cancer
- NCCN guideline: Esophageal and esophagogastric junction cancers
- NCCN guideline: Occult primary
- NCCN guideline: Central nervous system cancer
- NCCN guideline: Biliary tract cancer
- NCCN guideline: Thyroid carcinoma
- NCCN guideline: Ampullary adenocarcinoma
- NCCN guideline: Bladder cancer
- NCCN guideline: Colon cancer
- NCCN guideline: B-cell lymphomas
- NCCN guideline: Uterine neoplasms
- NCCN guideline: Primary cutaneous lymphomas
- NCCN guideline: Rectal cancer

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- NCCN guideline: Chronic lymphocytic leukemia/Small lymphocytic lymphoma
- NCCN guideline: Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
- NCCN guideline: Pancreatic adenocarcinoma
- NCCN guideline: Head and neck cancers
- NCCN guideline: Kidney cancer
- NCCN guideline: Vaginal cancer
- NCCN guideline: Peritoneal mesothelioma
- NCCN guideline: Pleural mesothelioma

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

- Cutaneous melanoma
- Non-small cell lung cancer
- Head and neck cancer
- Classical Hodgkin lymphoma
- Urothelial carcinoma
- Anaplastic thyroid carcinoma
- Follicular, Hurthle cell, or papillary thyroid carcinoma
- Colorectal cancer
- Merkel cell carcinoma
- Gastric cancer
- Esophageal cancer and esophagogastric junction cancer
- Cervical cancer
- Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
- Uveal melanoma
- Testicular cancer
- Endometrial carcinoma
- Anal carcinoma
- Central Nervous System (CNS) brain metastases
- Primary mediastinal large B-cell lymphoma
- Pancreatic adenocarcinoma
- Biliary tract cancers
- Hepatocellular carcinoma
- Renal cell carcinoma
- Vulvar cancer
- Thymic carcinoma
- Mycosis Fungoides/Sezary syndrome
- Anaplastic large cell lymphoma (ALCL)
- Extranodal NK/T-cell lymphoma
- Gestational trophoblastic neoplasia
- Neuroendocrine and Adrenal Tumors
- Prostate cancer
- Cutaneous squamous cell skin cancer

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- Occult primary cancer
- Small bowel adenocarcinoma
- Breast cancer
- Bone cancer
- Histologic (Richter) transformation to diffuse large B-cell lymphoma
- Penile cancer
- Soft tissue sarcoma
- Uterine sarcoma
- Ampullary Adenocarcinoma
- Small cell lung cancer
- Pediatric Diffuse High-Grade Gliomas
- Kaposi Sarcoma
- Vaginal Cancer
- Pleural or peritoneal mesothelioma

Explanation of Rationale

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

Support for the compendial uses in summary of evidence 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).

References

1. Keytruda [package insert]. Rahway, NJ: Merck Sharp & Dohme LLC; July 2025.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed August 19, 2025.

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