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P&T Date: 04/10/2025

Keytruda® (pembrolizumab)

HCPCS: J9271

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. Treatment must follow the FDA approved indications or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1 or 2A recommendation
      i. Must be used with concomitant treatment according to FDA indication or NCCN Category 1 or 2A recommendation
   b. Prescribed by or in consultation with an oncologist or hematologist
   c. No prior failure of a programmed death receptor-1 (PD-1) inhibitor
   d. Patient is not receiving therapy for a chronic condition, such as an autoimmune disease, that requires treatment with a systemic immunosuppressant
   e. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the WyoBlue Advantage utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time
   c. Renewal Criteria:
      i. Treatment continued until unacceptable toxicity or disease progression occurs
      ii. Renewal beyond 24 months of total therapy will be considered according to FDA approved drug labelling
      iii. Metastatic non-small cell lung cancer: Treatment until unacceptable toxicity or disease progression for up to a total of 24 months of therapy

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

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Background Information:

- Keytruda is a programmed death receptor-1 (PD-1)-blocking antibody indicated for the following:
    - For the treatment of patients with unresectable or metastatic melanoma
    - For the adjuvant treatment of adult and pediatric (12 years and older) patients with stage IIB, IIC, or III melanoma following complete resection
    - In combination with pemetrexed and platinum chemotherapy, as first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations
    - In combination with carboplatin and either paclitaxel or paclitaxel protein-bound, as first-line treatment of patients with metastatic squamous NSCLC
    - As a single agent 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
    - As a single agent 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
    - For the treatment of patients with resectable (tumors ≥ 4 cm or node positive) NSCLC in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery
    - As a single agent, for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC
    - In combination with pemetrexed and platinum chemotherapy, as first-line treatment of adult patients with unresectable advanced or metastatic pleural mesothelioma (MPM)
    - In combination with platinum and fluorouracil for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell cancer (HNSCC)
    - As a single agent 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
    - As a single agent for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy
    - For the treatment of adult patients with relapsed or refractory classic Hodgkin lymphoma (cHL)

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- For the treatment of pediatric patients with refractory cHL or cHL that has relapsed after 2 or more lines of therapy

- For the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma (PMBCL) or who have relapsed after 2 or more prior lines of therapy

- In combination with enfortumab vedotin, for the treatment of adult patients with locally advanced or metastatic urothelial cancer

- For the treatment of patients with locally advanced or metastatic urothelial carcinoma who

    - Are not eligible for any platinum-containing chemotherapy OR

    - Have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

- 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

- 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

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

- For the treatment of 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 in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, as first-line treatment

- In combination with fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma

- 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 OR

    - As a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1 (CPS ≥10) as determined by an FDA-approved test

- In combination with chemoradiotherapy, for the treatment of patients with FIGO 2014 stage III-IVA cervical cancer

- 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

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- As a single agent for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test

- 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

- In combination with gemcitabine and cisplatin, for the treatment of patients with locally advanced unresectable or metastatic biliary tract cancer (BTC)

- For the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC)

- In combination with axitinib, for the first-line treatment of patients with advanced renal cell carcinoma (RCC)

- In combination with lenvatinib, for the first-line treatment of adult patients with advanced RCC

- 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

- 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

- In combination with lenvatinib, for the treatment of patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

- As a single agent, 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

- 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

- For the treatment of patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced sCSS that is not curable by surgery or radiation

- 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

- In combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 10] as determined by an FDA approved test

- The National Comprehensive Cancer Network (NCCN) guidelines category 1 and 2A recommendations are based on uniform NCCN consensus that the recommendations are appropriate. Treatment regimens have been studied and shown to be efficacious when administered as listed in the guidelines. Category 2B and 3 recommendations do not

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have a high level of evidence to support use and also do not have a uniform consensus from the NCCN panel that the recommendations are appropriate.

- There are no studies to support use of Keytruda following failure. NCCN treatment guidelines also do not recommend use of Keytruda or other PD-L1 checkpoint inhibitors following a previous failure.

- Keytruda has not been studied in patients on chronic immunosuppressant therapy and therefore, should not be used in patients on chronic immunosuppressants.

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Policy History		
#	Date	Change Description
1.0	Initial Effective Date: 01/01/2026	New policy

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

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