pembrolizumab (Keytruda)

Medicare Part B Drug Policy

- Medicare coverage is limited to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury (and within the scope of a Medicare benefit category).
- Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50, describes national policy regarding Medicare guidelines for coverage of drugs and biologicals.
- Blue Shield of California (BSC) follows Medicare statutes, regulations, National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and policy articles for determining coverage for Part B drug requests when applicable.
- BSC Medicare Part B Drug Policies will be used when coverage criteria are not fully established or there is an absence of any applicable Medicare statutes, regulations, NCDs or LCDs.

Drug Details

USP Category: ANTINEOPLASTICS
Mechanism of Action: Human programmed death receptor-1 (PD-1) blocking antibody
HCPCS:
J9271:Injection, pembrolizumab, 1 mg
How Supplied:
100 mg (single-use vial)

Condition(s) listed in policy (see coverage criteria for details)

- Adrenocortical Carcinoma
- Anal Cancer
- Anaplastic Large Cell Lymphoma (ALCL), Cutaneous
- Anaplastic Thyroid Carcinoma
- Appendiceal Carcinoma or Colorectal Cancer
- Biliary Tract Cancers
- Breast Cancer (Triple-Negative)
- Cervical Cancer
- Chronic Lymphocytic Leukemia
- Cutaneous Squamous Cell Carcinoma
- Endometrial Cancer
- Esophageal Cancer
- Esophagogastric Junction (EGJ) Cancer
- Extranodal NK/T-cell Lymphoma, nasal type
- Gastric Cancer
- Gestational Trophoblastic Neoplasia
- Head and Neck Cancers
- Hepatocellular Carcinoma
- Hodgkin Lymphoma, Classical
- Kaposi Sarcoma
- Melanoma: Cutaneous

- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal or Pleural
- Mycosis Fungoides or Sezary Syndrome
- Non-Muscle Invasive Bladder Cancer (NMIBC)
- Non-small Cell Lung Cancer
- Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
- Primary Mediastinal Large B-Cell Lymphoma (PMBCL)
- Renal Cell Carcinoma
- Small Bowel Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Solid Tumors, dMMR/ MSI-H or TMB-H
- Thymic Carcinoma
- Urothelial Carcinoma
- Vaginal Cancer
- Vulvar Cancer

Any request for a condition not listed in policy must meet the definition of a medically accepted indication. Section 1861(t)(2)(B) of the Act defines "medically-accepted indication," as any use of a prescription drug or biological product which is approved under the Federal Food, Drug, and Cosmetic Act, or the use of which is supported by one or more citations included (or approved for inclusion) in one or more of the CMS approved compendia.

Special Instructions and Pertinent Information

Provider must submit documentation (such as office chart notes, lab results or other clinical information) to ensure the member has met all medical necessity requirements.

Coverage Criteria

The following condition(s) require Prior Authorization/Preservice:

Adrenocortical Carcinoma

Meets medical necessity if all the following are met:

1. Disease is locoregional unresectable or metastatic
2. Being used with or without mitotane

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:

yearly

ICD-10:

C7B.8, Z85.858

Anal Cancer

Meets medical necessity if all the following are met:

1. Used for subsequent treatment of metastatic cancer
2. Being used as a single agent

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:

yearly

ICD-10:

C21.0, C21.1, C21.2, C21.8

Anaplastic Large Cell Lymphoma (ALCL), Cutaneous

Meets medical necessity if all the following are met:

1. Being used for primary cutaneous ALCL with multifocal lesions, or cutaneous ALCL with regional node (N1)
2. Disease is relapsed or refractory
3. Being used as a single agent

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:

yearly

ICD-10:

C86.6

Anaplastic Thyroid Carcinoma

Meets medical necessity if all the following are met:

1. Disease is metastatic
2. Meets ONE of the following:
    1. Used as a single agent
    2. Used in combination with lenvatinib

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:

yearly

ICD-10:

C73, Z85.850

Appendiceal Carcinoma or Colorectal Cancer

Meets medical necessity if all the following are met:

1. Patient has defective mismatch repair/high microsatellite instability (dMMR/ MSI-H) or polymerase epsilon/delta [POLE/POLD1] mutation
2. Being used as a single agent

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C18.0, C18.1, C78.6, C78.7

Biliary Tract Cancers
Meets medical necessity if all the following are met:

1. Being used for one of the following:
   a. Gallbladder cancer
   b. Intrahepatic cholangiocarcinoma
   c. Extrahepatic cholangiocarcinoma
2. Disease is locally advanced unresectable, resected gross residual (R2), or metastatic
3. Being used in combination with gemcitabine and cisplatin

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C22.1, C23, C24.0, C24.8, C24.9

Breast Cancer (Triple-Negative)
Meets medical necessity if all the following are met:

1. HER2-negative
2. HR negative (ER and PR negativity)
3. Meets ONE of the following:
   a. Used for neoadjuvant and adjuvant treatment
   b. Used for inflammatory breast cancer and ALL of the following:
      1. No response to preoperative systemic therapy
      2. Used in combination with chemotherapy
      3. PD-L1 CPS ≥10
   c. Recurrent unresectable or metastatic disease and ALL the following:

i. Used in combination with chemotherapy
ii. PD-L1 CPS ≥10

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
Neoadjuvant: 24 weeks (8 doses of 200 mg every 3 weeks or 4 doses of 400 mg every 6 weeks)
Adjuvant: 27 weeks (9 doses of 200 mg every 3 weeks or 5 doses of 400 mg every 6 weeks)
Recurrent unresectable or metastatic: yearly

ICD-10:
C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229, C50.311, C50.312, C50.319, C50.321, C50.322, C50.329, C50.411, C50.412, C50.419, C50.421, C50.422, C50.429, C50.511, C50.512, C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929

Cervical Cancer
Meets medical necessity if all the following are met:
1. ONE of the following:
   a. Disease is PD-L1 positive (combined positive score [CPS] ≥1) and ALL the following:
      i. Persistent, recurrent, or metastatic disease
      ii. ONE of the following:
         1. Being used as a single agent for second-line or subsequent treatment after chemotherapy for recurrent or metastatic disease
         2. Being used in combination with cisplatin or carboplatin, paclitaxel, and with or without bevacizumab
   b. Disease is Stage III-IV and being used in combination with chemoradiotherapy

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C53.0, C53.1, C53.8, C53.9, C79.89, C79.9, Z80.49

Chronic Lymphocytic Leukemia
Meets medical necessity if all the following are met:
1. Histologic (Richter) transformation to diffuse large B-cell lymphoma from chronic lymphocytic leukemia
2. Meets ONE of the following:
   a. Being used as a single agent
   b. Bring used in combination with ibrutinib

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C83.00, C83.01, C83.02, C83.03, C83.04, C83.05, C83.06, C83.07, C83.08, C83.09, C83.30, C83.31, C83.32, C83.33, C83.34, C83.35, C83.36, C83.37, C83.38, C83.39, C91.10, C91.12

Cutaneous Squamous Cell Carcinoma
Meets medical necessity if all the following are met:

1. Recurrent, locally advanced, or metastatic disease
2. Being used as a single agent

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C44.02, C44.121, C44.1221, C44.1222, C44.1291, C44.1292, C44.221, C44.222, C44.229, C44.320, C44.321, C44.329, C44.42, C44.520, C44.521, C44.529, C44.621, C44.622, C44.629, C44.721, C44.722, C44.729, C44.82, C44.92

Endometrial Cancer
Meets medical necessity if all the following are met:

1. ONE of the following:
    a. Being used as a single agent therapy and ALL of the following:
        i. Disease has progressed on one or more prior lines of systemic therapy
        ii. Patient has defective mismatch repair or high microsatellite instability
    b. Being used in combination with carboplatin and paclitaxel for stage III or IV (metastatic), or recurrent disease
    c. Being used in combination with Lenvima and patient does not have defective mismatch repair or high microsatellite instability

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C54.8, C54.9, C55

Esophageal Cancer

Meets medical necessity if all the following are met:

1. Unresectable locally advanced, recurrent, or metastatic disease, or patient is not a surgical candidate, and ONE of the following:
    a. Being used in combination with a fluoropyrimidine (fluorouracil or capecitabine) and a platinum-containing (oxaliplatin or cisplatin) chemotherapy
    b. Being used as a single agent for esophageal squamous cell carcinoma, and ALL of the following:
        i. PD-L1 CPS≧ 10
        ii. Disease progression on 1 or more prior lines of systemic therapy

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:

yearly

ICD-10:

C15.3-C15.5, C15.8, C15.9, C16.0, D37.8, D37.9, Z85.00, Z85.01

Esophagogastric Junction (EGJ) Cancer

Meets medical necessity if all the following are met:

1. Unresectable locally advanced, recurrent, or metastatic disease, or patient is not a surgical candidate, and ONE of the following:
    1. Being used in combination with a fluoropyrimidine (fluorouracil or capecitabine) and a platinum-containing (oxaliplatin or cisplatin) chemotherapy
    2. Patient has HER2 positive EGJ adenocarcinoma and ALL of the following:
        1. Presence of HER2 positivity
        2. PD-L1 CPS≧1
        3. Being used as first-line treatment
        4. Being used in combination with trastuzumab, fluoropyrimidine, and a platinum-containing chemotherapy
    3. Patient has HER2 negative EGJ adenocarcinoma and ALL of the following:
        1. HER2 negative disease
        2. Being used as first-line treatment
        3. Being used in combination with fluoropyrimidine and platinum-containing chemotherapy

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:

yearly

ICD-10:

C15.3-C15.5, C15.8, C15.9, C16.0, D37.8, D37.9, Z85.00, Z85.01

Extranodal NK/T-cell Lymphoma, nasal type

Meets medical necessity if all the following are met:

1. Relapsed or refractory disease
2. Being used as a single agent

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:

yearly

ICD-10:

C84.Z0, C84.Z1, C84.Z2, C84.Z3, C84.Z4, C84.Z5, C84.Z6, C84.Z7, C84.Z8, C84.Z9, C86.0

Gastric Cancer

Meets medical necessity if all the following are met:

1. Early-stage or unresectable locoregional disease and ONE of the following:
   a. Patient has HER2 positive disease and meets ALL of the following:
      i. Presence of HER2 positivity
      ii. PD-L1 CPS≥1
      iii. Being used in combination with trastuzumab, fluoropyrimidine (fluorouracil or capecitabine), and platinum-containing (oxaliplatin or cisplatin) regimen
   b. Patient has HER2 negative disease and ALL of the following:
      i. HER2 negative disease
      ii. PD-L1 CPS≥10
      iii. Being used in combination with trastuzumab and fluoropyrimidine and platinum-containing regimen
2. Unresectable locally advanced, recurrent, or metastatic disease, or patient is not a surgical candidate, and ONE of the following:
   a. Patient has HER2 positive disease and ALL of the following:
      i. Presence of HER2 positivity
      ii. PD-L1 CPS≥1
      iii.
         1. Being used as first-line treatment
      iv. Being used in combination with trastuzumab, fluoropyrimidine, and a platinum-containing chemotherapy
      v. Patient has HER2 negative disease and ALL of the following:
         i. HER2 negative disease
         ii. Being used as first-line treatment
         iii. Being used in combination with fluoropyrimidine and platinum-containing chemotherapy

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C15.8, C15.9, C16.8, C16.9, D37.1, D37.8, D37.9, Z85.00, Z85.01

Gestational Trophoblastic Neoplasia
Meets medical necessity if all the following are met:

1. Being used as single-agent therapy
2. Disease is multiagent chemotherapy-resistant

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C58, D39.2

Head and Neck Cancers
Meets medical necessity if all the following are met:

1. Disease is unresectable, recurrent, persistent, or metastatic, and ONE of the following:
    a. Disease is non-nasopharyngeal cancer and ONE of the following:
        i. Being used as a single agent and ONE of the following:
            1. For first-line treatment or subsequent treatment if not previously used and patient has a PD-L1 CPS ≥1
            2. As subsequent line treatment and ALL of the following:
                a. After disease progression on or after platinum-containing chemotherapy
                b. Patient has not received prior treatment with PD-1/ PD-L1 immune checkpoint inhibitor therapy
        ii. Being used in combination with ONE of the following:
            1. Platinum and fluorouracil (FU) or docetaxel
            2. Platinum and paclitaxel
            3. Erbitux (cetuximab)
    b. Disease is nasopharyngeal cancer and being used in combination with cisplatin and gemcitabine

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C00.8, C00.9, C02.8, C02.9, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8, C04.9, C05.0, C05.1, C05.8, C05.9, C06.0, C06.2, C06.80, C06.89, C06.9, C09.0, C09.1, C09.8, C09.9, C10.8, C10.9, C12, C13.8, C13.9, C14.0, C14.2, C14.8, C31.0, C31.1, C32.8, C32.9, C44.00, C44.02, C44.09, C76.0, C77.0, D37.01, D37.02, D37.05, D37.09, D38.0, D38.5, D38.6

Hepatocellular Carcinoma
Meets medical necessity if all the following are met:
1. Disease has progressed on or after prior systemic therapy
2. Being used as a single agent
3. Patient has not received prior treatment with a PD-1/PD-L1-containing regimen

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C22.0, C22.8, C22.9

Hodgkin Lymphoma, Classical
Meets medical necessity if all the following are met:
1. ONE of the following:
    a. Being used as a single agent
    b. Being used in combination with GVD (gemcitabine, vinorelbine, liposomal doxorubicin)
    c. Being used in combination with ICE (ifosfamide, carboplatin, etoposide)
2. ONE of the following:
    a. Disease has relapsed, refractory or progressive
    b. Being used as palliative treatment in adults greater than 60 years of age

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C81.10, C81.11, C81.12, C81.13, C81.14, C81.15, C81.16, C81.17, C81.18, C81.19, C81.20, C81.21, C81.22, C81.23, C81.24, C81.25, C81.26, C81.27, C81.28, C81.29, C81.30, C81.31, C81.32, C81.33, C81.34, C81.35, C81.36, C81.37, C81.38, C81.39, C81.40, C81.41, C81.42, C81.43, C81.45, C81.46, C81.47, C81.48, C81.49, C81.70, C81.71, C81.72, C81.73, C81.74, C81.75, C81.76, C81.77, C81.78, C81.79, C81.90, C81.91, C81.92, C81.94, C81.95, C81.96, C81.97, C81.98, C81.99, Z85.71

Kaposi Sarcoma

Meets medical necessity if all the following are met:

1. Endemic or classic subtype
2. Relapsed/refractory advanced cutaneous, oral, visceral, or nodal disease
3. Being used as a single agent for subsequent therapy

Covered Doses:
200 mg given intravenously every 3 weeks for 8 cycles (8 doses)

Coverage Period:
6 months

ICD-10:
C46.0, C46.1, C46.2, C46.3, C46.4, C46.50, C46.51, C46.52, C46.7, C46.9

Melanoma: Cutaneous

Meets medical necessity if all the following are met:

1. Meets ONE of the following:
   a. Single agent for neoadjuvant treatment of limited resectable disease of ONE of the following:
      i. stage III disease with clinical satellite/in-transit metastases
      ii. local satellite/in-transit recurrence,
   b. Adjuvant treatment of disease as a single agent
   c. Metastatic or unresectable disease and meets ONE of the following:
      i. Used as a single agent
      ii. Used in combination with low-dose ipilimumab (1 mg/kg) or lenvatinib, and has had disease progression on an anti-PD-1/anti-PD-L1 immunotherapy drug
      iii. Used in combination with Tafinlar and Mekinist for BRAF V600 activating mutation as subsequent or re-induction therapy

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
Neo-adjuvant: 3 cycles
Adjuvant: 1 year
Metastatic or unresectable: yearly

ICD-10:
C43.0, C43.30, C43.31, C43.39, C43.4, C43.51, C43.52, C43.8, C43.9

Melanoma: Uveal

Meets medical necessity if all the following are met:

1. Disease is unresectable or metastatic
2. Being used as single agent therapy

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C69.30, C69.31, C69.32, C69.40, C69.41, C69.42, C69.60, C69.61, C69.62

Merkel Cell Carcinoma
Meets medical necessity if all the following are met:

1. Locally advanced, recurrent or metastatic (includes disseminated) disease
2. Being used as a single agent

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C4A.0, C4A.30, C4A.31, C4A.39, C4A.4

Mesothelioma: Peritoneal or Pleural
Meets medical necessity if all the following are met:

1. Being used as first-line treatment
2. Being used in combination with pemetrexed and platinum (cisplatin, carboplatin) chemotherapy

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C45.0, C45.1, C45.2, C45.7, C45.9

Mycosis Fungoides or Sezary Syndrome
Meets medical necessity if all the following are met:

1. Not being used in combination with other systemic therapies

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C84.00, C84.01, C84.02, C84.03, C84.04, C84.05, C84.06, C84.07, C84.08, C84.09, C84.10, C84.11, C84.12, C84.13, C84.14, C84.15, C84.16, C84.17, C84.18, C84.19

Non-Muscle Invasive Bladder Cancer (NMIBC)
Meets medical necessity if all the following are met:

1. Diagnosis of high-risk non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS)
2. Patient did not respond to Bacillus Calmette-Guerin (BCG) therapy
3. Being used as a single agent

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
D09.0, Z85.51

Non-small Cell Lung Cancer
Meets medical necessity if all the following are met:

1. ONE of the following:
    a. Being used in combination with platinum-containing chemotherapy as neoadjuvant treatment followed by single agent adjuvant treatment after surgery
    b. Being used as a single agent for adjuvant treatment following previous adjuvant chemotherapy
    c. Disease is advanced, recurrent, or metastatic and ONE of the following:
        i. Single agent use
        ii. In combination with either carboplatin or cisplatin, and either paclitaxel or Abraxane for squamous histology
        iii. In combination with either carboplatin or cisplatin, and pemetrexed for nonsquamous histology
        iv. Maintenance treatment and ONE of the following:
            1. In combination with Alimta after treatment with Keytruda, pemetrexed, AND carboplatin/cisplatin for nonsquamous histology
            2. As a single agent after treatment with Keytruda, Abraxane/paclitaxel and carboplatin/cisplatin for squamous histology

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C33, C34.00, C34.01, C34.02, C34.10, C34.11, C34.12, C34.2, C34.30, C34.31, C34.32, C34.80, C34.81, C34.82, C34.90, C34.91, C34.92, Z85.118

Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
Meets medical necessity if all the following are met:

1. Being used for platinum-resistant persistent disease or recurrence
2. Being used in combination with oral cyclophosphamide and bevacizumab

Covered Doses:
200 mg given intravenously every 3 weeks

Coverage Period:
yearly

ICD-10:
C48.1, C48.2, C48.8, C56.1, C56.2, C56.3, C56.9, C57.3, C57.4, Z85.43

Primary Mediastinal Large B-Cell Lymphoma (PMBCL)
Meets medical necessity if all the following are met:

1. Meets ONE of the following:
    a. Being used as a single agent for relapsed or refractory disease
    b. Being used in combination with Adcetris as consolidation/additional therapy in patient with partial response after therapy for relapsed or refractory disease in pediatric PMBCL

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C83.90, C83.91, C83.92, C83.93, C83.94, C83.95, C83.96, C83.97, C83.98, C83.99, C85.20, C85.21, C85.22, C85.23, C85.24, C85.25, C85.26, C85.27, C85.28, C85.29

Renal Cell Carcinoma
Meets medical necessity if all the following are met:

1. Either of the following:
    a. Adjuvant treatment following nephrectomy and being used as a single agent
    b. Disease is locally advanced, metastatic, or relapsed/recurrent and ONE of the following:
        i. Being used as a single agent for non-clear cell histology
        ii. Used in combination with Inlyta (axitinib) or Lenvima (lenvatinib)

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C64.1, C64.2, C64.9, C65.1, C65.2, C65.9, Z85.528

Small Bowel Adenocarcinoma
Meets medical necessity if all the following are met:
1. Advanced or metastatic disease
2. Presence of has defective mismatch repair/high microsatellite instability (dMMR/ MSI-H) or polymerase epsilon/delta [POLE/POLD1] mutation
3. Patient has not received prior treatment with PD-1/ PD-L1 immune checkpoint inhibitor therapy
4. Being used as a single agent

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C17.0, C17.1, C17.2, C17.3, C17.8, C17.9, Z85.068

Small Cell Lung Cancer
Meets medical necessity if all the following are met:
1. Used as single agent
2. ONE of the following:
   a. Primary progressive disease,
   b. Relapsed disease and relapse did not occur while receiving maintenance therapy with Imfinzi or Tecentriq

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C79.31, C79.51, C79.52, C7A.1

Soft Tissue Sarcoma
Meets medical necessity if all the following are met:
1. ONE of the following:
   a. Alveolar soft part sarcoma, and being used as a single agent or in combination with Inlyta (axitinib)

b. Cutaneous angiosarcoma, and being used as a single agent
c. Undifferentiated pleomorphic sarcoma (UPS), myxofibrosarcoma, dedifferentiated liposarcoma, pleomorphic rhabdomyosarcoma, or undifferentiated sarcomas and ALL of the following:
    i. Being used for unresectable, or metastatic (stage IV) disease
    ii. Being used as subsequent therapy

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C22.3, C47.0, C47.3, C47.4, C47.5, C47.6, C47.8, C47.9, Z85.831

Solid Tumors, dMMR/ MSI-H or TMB-H
Meets medical necessity if all the following are met:
1. Either of the following:
    a. Patient has defective mismatch repair (dMMR)/high microsatellite instability(MSI-H)
    b. Patient has tumor mutational burden-high (TMB-H) [10 mutations/megabase (mut/Mb)]
2. Being used as a single agent
3. ONE of the following:
    a. Initial therapy supported by NCCN
    b. Disease has progressed following prior treatment
    c. There are no alternative treatment options

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

Thymic Carcinoma
Meets medical necessity if all the following are met:
1. Being used as a single agent

Covered Doses:
- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:

C37, D15.0

Urothelial Carcinoma

Meets medical necessity if all the following are met:

1. Locally advanced, recurrent, or metastatic disease
2. EITHER of the following:
    a. Being used as a single agent, and ONE of the following:
        i. First line treatment in patients who are not eligible for any platinum-containing chemotherapy
        ii. Being used as subsequent therapy
    b. Being used in combination with Padcev (enfortumab vedotin) and patient is not eligible for cisplatin-containing chemotherapy

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:

yearly

ICD-10:

C61, C65.1, C65.2, C65.9, C66.1, C66.2, C66.9, C68.0, D09.0, Z85.51, Z85.59

Vaginal Cancer

Meets medical necessity if all the following are met:

1. Recurrent or metastatic disease
2. Being used in combination with paclitaxel, and cisplatin/carboplatin, with or without bevacizumab
3. Presence of PD-L1 positive tumor (combined positive score [CPS] ≥1)

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:

yearly

ICD-10:

C52

Vulvar Cancer

Meets medical necessity if all the following are met:

1. Advanced, recurrent, or metastatic disease
2. Squamous cell carcinoma or adenocarcinoma histology
3. Being used as a single agent
4. Disease progression on or after chemotherapy
5. Tumor has PD-L1 expression ≥ 1 on the CPS

Covered Doses:

- 200 mg given intravenously every 3 weeks
- 400 mg given intravenously every 6 weeks

Coverage Period:
yearly

ICD-10:
C51.8, C51.9

Additional Information

Summary of Evidence

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

1. The prescribing information for Keytruda
2. CMS approved compendium in accordance with the accepted compendia ratings listed:
   a. Micromedex DrugDex - Class I, Class IIa, of Class IIb
   b. American Hospital Formulary Service-Drug Information (AHFS-DI) - supportive narrative text
   c. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium - Category 1 or 2A
   d. Lexi-Drugs – "Use: Off-Label" and rated as "Evidence Level A" (cancer indications only)
   e. Clinical Pharmacology - supportive narrative text (cancer indications only)
3. NCCN Guideline: Ampullary adenocarcinoma
4. NCCN Guideline: Anal carcinoma
5. NCCN Guideline: B-cell lymphomas
6. NCCN Guideline: Biliary tract cancers
7. NCCN Guideline: Bladder cancer
8. NCCN Guideline: Bone cancer
9. NCCN Guideline: Breast cancer
10. NCCN Guideline: Central nervous system cancers
11. NCCN Guideline: Cervical cancer
12. NCCN Guideline: Chronic lymphocytic leukemia/small lymphocytic lymphoma
13. NCCN Guideline: Colon cancer
14. NCCN Guideline: Esophageal and esophagogastric junction cancers
15. NCCN Guideline: Gastric cancer
16. NCCN Guideline: Gestational trophoblastic neoplasia
17. NCCN Guideline: Head and neck cancers
18. NCCN Guideline: Hepatocellular carcinoma
19. NCCN Guideline: Hodgkin lymphoma
20. NCCN Guideline: Kaposi sarcoma
21. NCCN Guideline: Kidney cancer
22. NCCN Guideline: Melanoma: cutaneous
23. NCCN Guideline: Melanoma: uveal
24. NCCN Guideline: Merkel cell carcinoma
25. NCCN Guideline: Mesothelioma: Pleural
26. NCCN Guideline: Mesothelioma: Peritoneal

27. NCCN Guideline: Neuroendocrine and adrenal tumors
28. NCCN Guideline: Non-small cell lung cancer
29. NCCN Guideline: Occult primary
30. NCCN Guideline: Ovarian cancer/fallopian tube cancer/primary peritoneal cancer
31. NCCN Guideline: Pancreatic adenocarcinoma
32. NCCN Guideline: Pediatric aggressive mature B-cell lymphomas
33. NCCN Guideline: Pediatric central nervous system cancers
34. NCCN Guideline: Pediatric Hodgkin lymphoma
35. NCCN Guideline: Penile cancer
36. NCCN Guideline: Primary cutaneous lymphomas
37. NCCN Guideline: Prostate cancer
38. NCCN Guideline: Rectal cancer
39. NCCN Guideline: Small bowel adenocarcinoma
40. NCCN Guideline: Small cell lung cancer
41. NCCN Guideline: Soft tissue sarcoma
42. NCCN Guideline: Squamous cell skin cancer
43. NCCN Guideline: T-cell lymphomas
44. NCCN Guideline: Testicular cancer
45. NCCN Guideline: Thymomas and thymic carcinomas
46. NCCN Guideline: Thyroid carcinoma
47. NCCN Guideline: Uterine neoplasms
48. NCCN Guideline: Vaginal cancer
49. NCCN Guideline: Vulvar cancer

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:

- Adrenocortical carcinoma
- Anal cancer
- Anaplastic large cell lymphoma (ALCL), cutaneous
- Appendiceal carcinoma or colorectal cancer
- Biliary tract cancer (gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinomas)
- Breast cancer
- Cervical cancer
- Cutaneous squamous cell carcinoma
- Endometrial cancer
- Esophageal Cancer, esophagogastric junction (EGJ) cancer, and gastric cancer
- Extranodal NK/T-cell lymphoma, nasal type
- Gestational trophoblastic neoplasia
- Head and neck cancers
- Hepatocellular carcinoma
- Histologic (Richter) Transformation to Diffuse Large B-cell Lymphoma from Chronic Lymphocytic Leukemia
- Hodgkin lymphoma, classical

- Kaposi sarcoma
- Melanoma: cutaneous
- Melanoma: uveal
- Merkel cell carcinoma
- Mesothelioma: pleural
- Mesothelioma: peritoneal
- Mycosis fungoides or Sezary syndrome
- Non-muscle invasive bladder cancer (NMIBC)
- Non-small cell lung cancer (NSCLC)
- Ovarian cancer/fallopian tube cancer/primary peritoneal cancer
- Primary mediastinal large B-cell lymphoma
- Renal cell carcinoma
- Small bowel adenocarcinoma
- Small cell lung cancer
- Soft tissue sarcoma
- Solid Tumors, dMMR/ MSI-H or TMB-H
- Thymic carcinoma
- Urothelial Carcinoma
- Vulvar Cancer

Explanation of Rationale:

- Support for FDA-approved indications can be found in the manufacturer's prescribing information.
- Support for the listed indications is found in the National Comprehensive Cancer Network's (NCCN) Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drug and biologic medications 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).
    - Adrenocortical carcinoma
    - Anal cancer
    - Anaplastic large cell lymphoma (ALCL), cutaneous
    - Appendiceal carcinoma or colorectal cancer
    - Biliary tract cancer (gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinomas)
    - Breast cancer
    - Cervical cancer
    - Cutaneous squamous cell carcinoma
    - Endometrial cancer
    - Esophageal cancer, esophagogastric junction (EGJ) cancer, and gastric cancer
    - Extranodal NK/T-cell lymphoma, nasal type
    - Gestational trophoblastic neoplasia
    - Head and neck cancers
    - Hepatocellular carcinoma

- Histologic (Richter) Transformation to Diffuse Large B-cell Lymphoma from Chronic Lymphocytic Leukemia
- Hodgkin lymphoma, classical
- Kaposi sarcoma
- Melanoma: cutaneous
- Melanoma: uveal
- Merkel cell carcinoma
- Mesothelioma: Pleura
- Mesothelioma: Peritoneal
- Mycosis fungoides or Sezary syndrome
- Non-muscle invasive bladder cancer (NMIBC)
- Non-small cell lung cancer (NSCLC)
- Ovarian cancer/fallopian tube cancer/primary peritoneal cancer
- Primary mediastinal large B-cell lymphoma
- Renal cell carcinoma
- Small bowel adenocarcinoma
- Small cell lung cancer
- Soft tissue sarcoma
- Solid Tumors, dMMR/ MSI-H or TMB-H
- Thymic carcinoma
- Urothelial Carcinoma
- Vulvar Cancer

References

1. CMS Benefit Policy Manual. Chapter 15; § 50 Drugs and Biologicals
2. Medicare Coverage Database. Available at https://www.cms.gov/Medicare-Coverage-Database/search.aspx
3. Social Security Act (Title XVIII) Standard References, Sections: 1862(a)(1)(A) Medically Reasonable & Necessary; 1862(a)(1)(D) Investigational or Experimental; 1833(e) Incomplete Claim; 1861(t) (1) Drugs and Biologicals
4. AHFS. Available by subscription at http://www.lexi.com
5. DrugDex. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
6. Keytruda (pembrolizumab) [Prescribing information]. Merck & CO., inc.; Whitehouse Station, NJ. 2024.
7. National Comprehensive Cancer Network Drugs and Biologics Compendium. Keytruda (10/2024). Available at: www.nccn.org.
8. National Comprehensive Cancer Network. Anal Carcinoma (Version 1.2024). Available at: www.nccn.org.
9. National Comprehensive Cancer Network. B-Cell Lymphomas (Version 3.2024). Available at: www.nccn.org.
10. National Comprehensive Cancer Network. Biliary Tract Cancers (Version 4.2024). Available at: www.nccn.org.
11. National Comprehensive Cancer Network. Bladder Cancer (Version 4.2024). Available at: www.nccn.org.
12. National Comprehensive Cancer Network. Breast Cancer (Version 4.2024). Available at: www.nccn.org.

13. National Comprehensive Cancer Network. Cervical Cancer (Version 4.2024). Available at: www.nccn.org.
14. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (Version 1.2025). Available at: www.nccn.org.
15. National Comprehensive Cancer Network. Colon Cancer (Version 5.2024). Available at: www.nccn.org.
16. National Comprehensive Cancer Network. Esophageal and Esophagogastric Junction Cancers (Version 4.2024). Available at: www.nccn.org.
17. National Comprehensive Cancer Network. Gastric Cancer (Version 2.2024). Available at: www.nccn.org.
18. National Comprehensive Cancer Network. Gestational Trophoblastic Neoplasia (Version 2.2024). Available at: www.nccn.org.
19. National Comprehensive Cancer Network. Head and Neck Cancers (Version 4.2024). Available at: www.nccn.org.
20. National Comprehensive Cancer Network. Hepatocellular Carcinoma (Version 3.2024). Available at: www.nccn.org.
21. National Comprehensive Cancer Network. Hodgkin Lymphoma (Version 3.2024). Available at: www.nccn.org.
22. National Comprehensive Cancer Network. Kaposi Sarcoma (Version 1.2024). Available at: www.nccn.org.
23. National Comprehensive Cancer Network. Kidney Cancer (Version 2.2025). Available at: www.nccn.org.
24. National Comprehensive Cancer Network. Melanoma: Cutaneous (Version 3.2024). Available at: www.nccn.org.
25. National Comprehensive Cancer Network. Melanoma: Uveal (Version 1.2024). Available at: www.nccn.org.
26. National Comprehensive Cancer Network. Merkel Cell Carcinoma (Version 1.2024). Available at: www.nccn.org.
27. National Comprehensive Cancer Network. Mesothelioma: Pleural (Version 2.2024). Available at: www.nccn.org.
28. National Comprehensive Cancer Network. Mesothelioma: Peritoneal (Version 3.2024). Available at: www.nccn.org.
29. National Comprehensive Cancer Network. Neuroendocrine and Adrenal Tumors (Version 2.2024). Available at: www.nccn.org.
30. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer (Version 10.2024). Available at: www.nccn.org.
31. National Comprehensive Cancer Network. Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer (Version3.2024). Available at: www.nccn.org.
32. National Comprehensive Cancer Network. Pediatric Central Nervous System Cancers (Version 1.2024). Available at: www.nccn.org.
33. National Comprehensive Cancer Network. Pediatric Hodgkin Lymphoma (Version 1.2024). Available at: www.nccn.org.
34. National Comprehensive Cancer Network. Pediatric Aggressive Mature B-Cell Lymphomas (Version 2.2024). Available at: www.nccn.org
35. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas (Version 3.2024). Available at: www.nccn.org.

36. National Comprehensive Cancer Network. Rectal Cancer (Version 4.2024). Available at: www.nccn.org.
37. National Comprehensive Cancer Network. Small Bowel Adenocarcinoma (Version 5.2024). Available at: www.nccn.org.
38. National Comprehensive Cancer Network. Small Cell Lung Cancer (Version 2.2025). Available at: www.nccn.org.
39. National Comprehensive Cancer Network. Soft Tissue Sarcoma (Version 3.2024). Available at: www.nccn.org.
40. National Comprehensive Cancer Network. Squamous Cell Skin Cancer (Version 1.2024). Available at: www.nccn.org.
41. National Comprehensive Cancer Network. T-cell Lymphomas (Version 4.2024). Available at: www.nccn.org.
42. National Comprehensive Cancer Network. Thymomas and Thymic Carcinomas (Version 1.2024). Available at: www.nccn.org.
43. National Comprehensive Cancer Network. Thyroid Carcinoma (Version 4.2024). Available at: www.nccn.org.
44. National Comprehensive Cancer Network. Uterine Neoplasms Cancer (Version 3.2024). Available at: www.nccn.org.
45. National Comprehensive Cancer Network. Vaginal Cancer (Version 2.2025). Available at: www.nccn.org.
46. National Comprehensive Cancer Network. Vulvar Cancer (Version 4.2024). Available at: www.nccn.org.

Review History

Date of Last Annual Review: MM/dd/yyyy
Changes from previous policy version:

- New Part B drug policy

Blue Shield of California Medication Policy to Determine Medical Necessity Reviewed by P&T Committee