PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Injectable – Programmed Death Receptor-1) – Keytruda Prior Authorization Policy
- Keytruda® (pembrolizumab intravenous infusion – Merck)

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OVERVIEW

Keytruda, a human programmed death receptor-1 (PD-1) blocking antibody, is indicated for the treatment of the following indications:[1]

- **Breast cancer, triple-negative**, in the following situations:
  - In combination with chemotherapy for the treatment of patients with locally recurrent unresectable or metastatic disease whose tumors express programmed death-ligand 1 (PD-L1) [combined positive score {CPS} ≥ 10] as determined by an FDA-approved test.*
  - For the treatment of high-risk, early-stage disease in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.
- **Cervical cancer**, in the following situations:
  - In combination with chemotherapy, with or without bevacizumab, for persistent, recurrent, or metastatic disease whose tumor expresses PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
  - As a single agent, for treatment of patients with recurrent or metastatic disease with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
- **Classical Hodgkin lymphoma**, in the following situations:
  - For treatment of adult patients with relapsed or refractory disease.
  - For the treatment of pediatric patients with refractory disease, or disease that has relapsed after two or more prior lines of therapy.
- **Cutaneous squamous cell carcinoma,** treatment of patients with recurrent, metastatic disease or locally advanced disease that is not curable by surgery or radiation.
- **Endometrial cancer**, in the following situations:
  - In combination with Lenvima® (lenvatinib capsules), for the treatment of patients with advanced disease that is not microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.
  - As a single agent, for the treatment of patients with advanced disease that is MSI-H or dMMR as determined by an FDA-approved test, and who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.
- **Esophageal cancer**, treatment of patients with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) carcinoma (tumors with epicenter 1 to 5 centimeters above the GEJ) that is not amenable to surgical resection or definitive chemoradiation in the following situations:
  - In combination with platinum- and fluoropyrimidine-based chemotherapy.
  - 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.
- **Gastric cancer**, for the first-line treatment of patients with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive gastric or GEJ

adenocarcinoma, in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy.*

- **Head and neck squamous cell carcinoma**, in the following situations:
  - As a single agent for the treatment of recurrent or metastatic disease with disease progression on or after platinum-containing chemotherapy.
  - In combination with platinum and fluorouracil (FU) for the first-line treatment of patients with metastatic or with unresectable, recurrent disease.
  - As a single agent, for the first line treatment of patients with metastatic or with unresectable, recurrent disease whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
- **Hepatocellular carcinoma**, for treatment of patients who have been previously treated with Nexavar® (sorafenib tablets).*
- **Melanoma**, in the following situations:
  - For the treatment of patients with unresectable or metastatic disease.
  - As adjuvant treatment of patients ≥ 12 years of age with Stage IIB, IIC, or III melanoma following complete resection.
- **Merkel cell carcinoma**, for adult and pediatric patients with recurrent, locally advanced, or metastatic disease.*
- **Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)**, for treatment of adult and pediatric patients with unresectable or metastatic MSI-H or dMMR solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.*
  Limitation of Use: The safety and effectiveness of Keytruda in pediatric patients with MSI-H central nervous system cancers have not been established.
- **Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer,** for the treatment of patients with unresectable or metastatic disease.
- **Non-small cell lung cancer** (**NSCLC**), in the following situations:
  - As a single agent for the first-line treatment of patients whose tumors express PD-L1 (tumor proportion score [TPS] ≥ 1%) as determined by an FDA-approved test, with no epidermal growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation or for metastatic disease.
  - As a single agent for the treatment of patients with metastatic disease whose tumors express PD-L1 (TPS ≥ 1%) as determined by an FDA-approved test and 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.
  - In combination with Alimta® (pemetrexed intravenous infusion) and platinum-based chemotherapy, for the first-line treatment of patients with metastatic nonsquamous NSCLC with no *EGFR* or *ALK* genomic tumor aberrations.
  - In combination with carboplatin and either paclitaxel or Abraxane® (nab-paclitaxel intravenous infusion), for first-line treatment in metastatic squamous NSCLC.
- **Primary mediastinal large B-cell lymphoma** (PMBCL), for treatment of adult and pediatric patients with refractory disease, or who have relapsed after two or more prior lines of therapy.
  Limitation of Use: Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.
- **Renal cell carcinoma**, in the following situations:
  - In combination with Inlyta® (axitinib tablets) or Lenvima, for the first-line treatment of patients with advanced disease.

  - For adjuvant treatment of disease that is intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.
- **Tumor mutational burden-high (TMB-H) cancer**, treatment of adult and pediatric patients with unresectable or metastatic TMB-H (≥ 10 mutations/megabase) disease, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.*
  Limitation of Use: The safety and effectiveness of Keytruda in pediatric patients with TMB-H central nervous system cancers have not been established.
- **Urothelial carcinoma**, in the following situations:
  - Treatment of locally advanced or metastatic disease in patients who are not eligible for platinum-containing chemotherapy.
  - Treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
  - Treatment of Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer with carcinoma in situ with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

* This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Keytruda. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Keytruda as well as the monitoring required for adverse events and long-term efficacy, approval requires the medication to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Keytruda is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Breast Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):
   A) Patient is ≥ 18 years of age; AND
   B) Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
   Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.
   C) Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); AND
   Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
   D) Patient has triple-negative breast cancer (i.e., estrogen receptor-negative, progesterone receptor-negative, human epidermal growth factor receptor 2 [HER2]-negative); AND
   E) Patient meets ONE of the following (i or ii):
      i. Patient meets ALL of the following (a, b, and c):

a) Patient has recurrent unresectable (local or regional) or metastatic disease; AND
b) The medication is used in combination with chemotherapy; AND
c) Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 10; OR

ii. Patient has high-risk, early-stage disease; AND

F) The medication is prescribed by or in consultation with an oncologist.

2. Cervical Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):

A) Patient is ≥ 18 years of age; AND
B) Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.
C) Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); AND
Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
D) Patient has persistent, recurrent, or metastatic disease; AND
E) Patient's tumor expression for programmed death-ligand 1 (PD-L1), as determined by an approved test, has a combined positive score (CPS) ≥ 1; AND
F) The medication is prescribed by or in consultation with an oncologist.

3. Classic Hodgkin Lymphoma. Approve for 1 year if the patient meets BOTH of the following (A and B):

A) Patient meets ONE of the following (i or ii):
i. Patient meets BOTH of the following (a and b):
a) Patient is ≥ 18 years of age; AND
b) Patient has tried at least one systemic regimen; OR
Note: Examples of systemic regimens are ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) + rituximab, CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab, CVbP (cyclophosphamide, vinblastine, prednisolone) + rituximab, Adcetris (brentuximab vedotin intravenous infusion) + AVD (doxorubicin, vinblastine, dacarbazine).
ii. Patient meets BOTH of the following (a and b):
a) Patient is < 18 years of age; AND
b) Patient has relapsed or refractory disease; AND
B) The medication is prescribed by or in consultation with an oncologist.

4. Cutaneous Squamous Cell Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND
B) Patient has locally advanced, recurrent, or metastatic disease; AND
C) The disease is not curable by surgery or radiation; AND
D) The medication is prescribed by or in consultation with an oncologist.

5. Endometrial Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, F, and G):

A) Patient is ≥ 18 years of age; AND
B) Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.
C) Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); AND

Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.

D) The medication is used in combination with Lenvima (lenvatinib capsules); AND

E) Patient has progressed on at least one prior systemic therapy; AND
Note: Examples of systemic therapy are carboplatin, paclitaxel, docetaxel, cisplatin, doxorubicin, ifosfamide, everolimus, letrozole.

F) Patient is not a candidate for curative surgery or radiation; AND

G) The medication is prescribed by or in consultation with an oncologist.

6. Esophageal and Esophagogastric Junction Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):

A) Patient is ≥ 18 years of age; AND

B) Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.

C) Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); AND
Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.

D) Patient meets ONE of the following (i or ii):
- **i.** According to the prescriber, the patient is not a surgical candidate; OR
- **ii.** Patient has unresectable, recurrent, or metastatic disease; AND

E) Patient meets ONE of the following (i, ii, iii, or iv):
- **i.** Patient meets ALL of the following (a, b, and c):
  - **a)** Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 10; AND
  - **b)** The medication is used first-line; AND
  - **c)** The medication is used in combination with chemotherapy; OR
    Note: Examples of chemotherapy include cisplatin plus fluorouracil or capecitabine; and oxaliplatin plus fluorouracil or capecitabine.
- **ii.** Patient meets ALL of the following (a, b, and c):
  - **a)** Patient has squamous cell carcinoma; AND
  - **b)** Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 10; AND
  - **c)** Patient has tried at least one previous chemotherapy regimen; OR
    Note: Examples of chemotherapy regimens are fluoropyrimidine (fluorouracil or capecitabine) and oxaliplatin, fluoropyrimidine and cisplatin, paclitaxel with cisplatin or carboplatin, docetaxel with cisplatin.
- **iii.** Patient meets BOTH of the following (a and b):
  - **a)** Tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu positive; AND
  - **b)** Medication is used in combination with trastuzumab, cisplatin or oxaliplatin, and fluorouracil or capecitabine; OR
- **iv.** Patient meets ALL of the following (a, b, and c):
  - **a)** Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined score (CPS) ≥ 1; AND
  - **b)** Patient has tried at least two previous chemotherapy regimens; AND
    Note: Examples of chemotherapy regimens are fluoropyrimidine (fluorouracil or capecitabine) and oxaliplatin, fluoropyrimidine and cisplatin, paclitaxel with cisplatin or carboplatin, docetaxel with cisplatin.
  - **c)** If the patient's tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu positive, targeted therapy with trastuzumab has been tried; AND

F) The medication is prescribed by or in consultation with an oncologist.

7. **Gastric Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
     Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.
   - **C)** Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); AND
     Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
   - **D)** Patient meets one of the following (i or ii):
     - **i.** Patient meets ALL of the following (a, b, and c):
       - **a)** Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 1; AND
       - **b)** Patient has tried at least two previous chemotherapy regimens; AND
         Note: Examples of chemotherapy regimens are fluoropyrimidine (fluorouracil or capecitabine) and oxaliplatin, fluoropyrimidine and cisplatin, paclitaxel with cisplatin or carboplatin, docetaxel with cisplatin.
       - **c)** If the patient's tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu positive, targeted therapy with trastuzumab has been tried; OR
     - **ii.** Patient meets ALL of the following (a, b, and c):
       - **a)** Patient has locally advanced unresectable or metastatic disease; AND
       - **b)** Tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu positive; AND
       - **c)** Medication is used in combination with trastuzumab, cisplatin or oxaliplatin, and fluorouracil or capecitabine; AND
   - **E)** The medication is prescribed by or in consultation with an oncologist.

8. **Head and Neck Squamous Cell Carcinoma.** Approve for 1 year if the patients meets ALL of the following (A, B, C, D, E, and F):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
     Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.
   - **C)** Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); AND
     Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
   - **D)** Patient has recurrent, unresectable, or metastatic disease; AND
   - **E)** Patient meets ONE of the following (i or ii):
     - **i.** If the medication is used for first-line treatment, patient must meet ONE of the following (a or b):
       - **a)** Keytruda is used in combination with chemotherapy; OR
         Note: Examples of chemotherapy are cisplatin, carboplatin, fluorouracil, gemcitabine.
       - **b)** Keytruda is used as a single agent if the tumors are PD-L1-positive (combined positive score ≥ 1), as determined by an approved test.
     - **ii.** For subsequent therapy, patient has tried at least one platinum-containing chemotherapy regimen; AND
       Note: Examples of platinum-contain chemotherapy regimens are: cisplatin or carboplatin with Erbitux (cetuximab intravenous infusion), gemcitabine, or 5-fluorouracil (5-FU).
   - **F)** The medication is prescribed by or in consultation with an oncologist.

9. **Hepatocellular Carcinoma, Including Hepatobiliary Cancers**. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):

A) Patient is ≥ 18 years of age; AND
B) Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.
C) Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); AND
Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
D) Patient has tried at least one tyrosine kinase inhibitor; AND
Note: Examples of tyrosine kinase inhibitors include Nexavar (sorafenib tablets) and Lenvima (lenvatinib capsules).
E) The medication is prescribed by or in consultation with an oncologist.

10. Melanoma. Approve for the duration noted below if the patient meets ALL of the following (A, B, and C):
Note: This includes cutaneous melanoma, brain metastases due to melanoma and uveal melanoma.
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
i. Approve for 1 year if the patient has unresectable, advanced, or metastatic melanoma; OR
ii. Approve for up to 1 year (total) if Keytruda will be used as adjuvant treatment; AND
Note: For example, in a patient with no evidence of disease following resection of node-positive disease, locoregional recurrence, or in transit recurrence.
C) The medication is prescribed by or in consultation with an oncologist.

11. Merkel Cell Carcinoma. Approve for 1 year if the patient meets BOTH of the following (A and B):
A) Patient has recurrent, locally advanced, or metastatic disease; AND
B) The medication is prescribed by or in consultation with an oncologist.

12. Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors. Approve for 1 year if the patient meets BOTH of the following (A and B):
Note**:** Examples of solid tumors with MSI-H or dMMR are adrenal gland, biliary tract cancers, breast cancer, cervical cancer, chondrosarcoma, colon or rectal cancer, endometrial carcinoma, esophageal or esophagogastric cancers, Ewing sarcoma, gallbladder carcinoma, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, occult primary (cancer of unknown primary), osteosarcoma, ovarian/fallopian tube/primary peritoneal, pancreatic adenocarcinoma, penile cancer, poorly differentiated neuroendocrine tumor, prostate cancer, small bowel adenocarcinoma, testicular cancer, vulvar cancer.
A) One of the following conditions applies (i, ii, iii, iv, v, vi, vii, or viii):
i. Patient has advanced or metastatic ampullary cancer; OR
ii. Patient has unresectable or metastatic colon or rectal cancer; OR
iii. Patient has unresectable or metastatic gallbladder cancer (including intra- and extra-hepatic cholangiocarcinoma); OR
iv. Patient has unresectable or metastatic head and neck squamous cell carcinoma; OR
v. Patient has persistent or recurrent ovarian/fallopian tube/primary peritoneal carcinoma; OR
vi. Patient has locally advanced or metastatic pancreatic adenocarcinoma; OR
vii. Patient has advanced or metastatic small bowel carcinoma; OR
viii. Patient meets BOTH of the following (a and b):
a) Patient has tried at least one prior systemic therapy for an MSI-H or dMMR solid tumor; AND
b) Patient has unresectable or metastatic disease; AND
B) The medication is prescribed by or in consultation with an oncologist.

13. Non-Small Cell Lung Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has recurrent, advanced, or metastatic disease; AND
- **C)** Patient meets ONE of the following (i, ii, or iii):
  - **i.** Patient meets BOTH of the following (a and b):
    - **a)** Keytruda is used as first-line or continuation maintenance therapy; AND
      Note: This is regardless of PD-L1 status.
    - **b)** The tumor is negative for actionable mutations; OR
      Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (*EGFR*) mutation, anaplastic lymphoma kinase (*ALK*) fusions, *NTRK* gene fusion-positive, *ROS1*, *BRAF V600E*, *MET 14* skipping mutation, *RET* rearrangement.
  - **ii.** Patient meets BOTH of the following (a and b):
    - **a)** Keytruda is used as first-line or subsequent therapy; AND
      Note: This is regardless of the PD-L1 status.
    - **b)** The tumor is positive for one of the following mutations [(1), (2), (3), (4), (5), or (6)]:
      - **(1)** Epidermal growth factor receptor (EGFR) exon 20 mutation; OR
      - **(2)** KRAS G12C mutation; OR
      - **(3)** BRAF V600E mutation; OR
      - **(4)** NTRK1/2/3 gene fusion; OR
      - **(5)** MET exon 14 skipping mutation; OR
      - **(6)** RET rearrangement; OR
  - **iii.** Keytruda is used as subsequent therapy and the patient meets ONE of the following (a, b, or c):
    - **a)** Patient meets BOTH of the following [(1) and (2)]:
      - **(1)** The tumor is epidermal growth factor receptor (EGFR) S768I, L861Q, and/or G719X mutation positive; AND
      - **(2)** The patient has received targeted drug therapy for the specific mutation; OR
        Note: Examples of targeted drug therapy include Gilotrif (afatinib tablet), Tagrisso (osimertinib tablet), erlotinib, Iressa (gefitinib tablet), or Vizimpro (dacomitinib tablet).
    - **b)** Patient meets BOTH of the following [(1) and (2)]:
      - **(1)** The tumor is ROS1 rearrangement positive; AND
      - **(2)** The patient has received targeted drug therapy for the specific mutation; OR
        Note: Examples of targeted drug therapy include Xalkori (crizotinib capsule), Rozlytrek (entrectinib capsule), or Zykadia (ceritinib tablet).
    - **c)** Patient meets ALL of the following [(1), (2), and (3)]:
      - **(1)** Patient has tried systemic therapy; AND
        Note: Examples of systemic chemotherapy include cisplatin, carboplatin, Alimta (pemetrexed intravenous infusion), Abraxane (paclitaxel albumin-bound intravenous infusion), gemcitabine, paclitaxel.
      - **(2)** Patient has not progressed on prior therapy with a programmed death-1 (PD-1)/PD-ligand 1 (PD-L1) inhibitor; AND
        Note: This includes previous therapy with either one of Keytruda, Opdivo (nivolumab intravenous infusion), or Tecentriq (atezolizumab intravenous infusion).
      - **(3)** If tumor is positive for an actionable mutation, the patient has received targeted drug therapy for the specific mutation; AND
        Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (*EGFR*) mutation, anaplastic lymphoma kinase (*ALK*) fusions, *NTRK* gene fusion positive, *ROS1*, *BRAF V600E*, *MET* exon 14 skipping mutation, *RET* rearrangement.

D) The medication is prescribed by or in consultation with an oncologist.

14. Primary Mediastinal Large B-Cell Lymphoma. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient has relapsed after, or is refractory to, at least two previous regimens; AND
  Note: Examples of previous regimens include autologous hematopoietic stem cell transplant (auto-HSCT), EPOCH-R (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, rituximab), RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone], RCEPP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone).
- **B)** The medication is prescribed by or in consultation with an oncologist.

15. Renal Cell Carcinoma. Approve for the duration noted below if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following (i, ii, or iii):
  - **i.** Approve for 1 year if the patient meets ALL of the following (a, b, and c):
    - **a)** The tumor has clear cell histology; AND
    - **b)** Patient has relapsed or metastatic disease; AND
    - **c)** The medication is used in combination with Inlyta (axitinib tablets) or Lenvima (lenvatinib capsules); OR
  - **ii.** Approve for 1 year if the patient meets ALL of the following (a, b, and c):
    - **a)** The tumor has non-clear cell histology; AND
    - **b)** Patient has relapsed or metastatic disease; AND
    - **c)** The medication is used as single-agent therapy; OR
  - **iii.** Approve for up to 1 year (total) if patient meets ALL of the following (a, b, c, and d):
    - **a)** Keytruda is used as adjuvant therapy; AND
    - **b)** The tumor has clear cell histology; AND
    - **c)** Patient has advanced disease; AND
    - **d)** The medication is used as single-agent therapy; AND
- **C)** The medication is prescribed by or in consultation with an oncologist.

16. Tumor Mutational Burden-High (TMB-H) Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient has unresectable or metastatic tumor mutational burden-high (≥ 10 mutations/megabase) solid tumor; AND
  Note: Examples of solid tumors are adrenal cancer, breast cancer, cervical cancer, cholangiocarcinoma (intrahepatic and extrahepatic), chondrosarcoma, chordoma, endometrial carcinoma, esophageal carcinoma, esophagogastric junction carcinoma, Ewing sarcoma, gallbladder cancer, gastric cancer, head and neck cancer, neuroendocrine cancer, osteosarcoma, ovarian/fallopian tube/primary peritoneal carcinoma, primary occult, salivary gland tumors, testicular cancer, thyroid cancer, uterine sarcoma, vulvar cancer.
- **B)** Patient has progressed on prior therapy; AND
- **C)** Patient has no satisfactory alternative treatment options; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

17. Urothelial Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following conditions (i, ii, or iii):
  - **i.** Patient has tried at least one platinum-based chemotherapy; OR
    Note: Cisplatin and carboplatin are platinum-based chemotherapies.

ii. According to the prescriber, patient is not eligible for platinum-based chemotherapy (i.e., with cisplatin and carboplatin); OR
Note: This is regardless of PD-L1 status.

iii. Patient meets both of the following (a and b):

a) Patient has non-muscle invasive bladder cancer; AND

b) Patient has tried Bacillus Calmette-Guerin (BCG) or intravesical chemotherapy; AND
Note: Examples of agents used as intravesical chemotherapy include mitomycin and gemcitabine.

C) The medication is prescribed by or in consultation with an oncologist.

Other Uses with Supportive Evidence

18. Adrenal Gland Tumor. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Patient has unresectable or metastatic adrenocortical carcinoma; AND

C) The medication is prescribed by or in consultation with an oncologist.

19. Anal Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Patient has received at least one other chemotherapy regimen; AND
Note: Examples of chemotherapy regimens are 5-fluorouracil (5-FU), cisplatin, carboplatin, paclitaxel, FOLFOX (oxaliplatin, leucovorin, and 5-FU).

C) The medication is prescribed by or in consultation with an oncologist.

20. Extranodal NK/T-Cell Lymphoma, Nasal Type. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Patient has received an asparaginase-based chemotherapy regimen; AND
Note: Examples of asparaginase-based chemotherapy are dexamethasone, ifosfamide, pegaspargase, etoposide; and gemcitabine, pegaspargase, oxaliplatin.

C) The medication is prescribed by or in consultation with an oncologist.

21. Gestational Trophoblastic Neoplasia. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Patient meets ONE of the following (i or ii):

i. Patient has tried at least one previous chemotherapy regimen for recurrent or progressive disease; OR
Note: Examples of chemotherapy regimens contain etoposide, cisplatin/carboplatin, paclitaxel, bleomycin, ifosfamide, methotrexate.

ii. Patient has high-risk disease; AND

C) The medication is prescribed by or in consultation with an oncologist.

22. Mycosis Fungoides/Sezary Syndrome. Approve for 1 year if the patient meets BOTH of the following (A and B):

A) Patient is ≥ 18 years of age; AND

B) The medication is prescribed by or in consultation with an oncologist.

23. Primary Cutaneous Anaplastic Large Cell Lymphoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND

B) Patient has relapsed or refractory disease; AND
C) Patient meets ONE of the following (i or ii):
  i. Patient has disease with multifocal lesions; OR
  ii. Patient has disease with regional node; AND
D) The medication is prescribed by or in consultation with an oncologist.

24. Small Cell Lung Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Keytruda is used as subsequent therapy; AND
C) The medication is prescribed by or in consultation with an oncologist.

25. Soft Tissue Sarcoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 18 years of age; AND
B) Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); AND
Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
C) Patient has alveolar soft part sarcoma; AND
D) The medication is prescribed by or in consultation with an oncologist.

26. Squamous Cell Skin Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i, ii, or iii):
  i. Patient meets BOTH of the following (a and b):
    a) Patient has locally advanced disease; AND
    b) According to the prescriber, curative surgery and curative radiation therapy are not feasible; OR
  ii. Patient meets BOTH of the following (a and b):
    a) Patient has unresectable, inoperable, or not fully resectable regional disease; AND
    b) According to the prescriber, curative radiation therapy is not feasible; OR
  iii. Patient meets BOTH of the following (a and b):
    a) Patient has regional recurrence or metastatic disease; AND
    b) According to the prescriber, curative radiation therapy or curative surgery are not feasible; AND
C) The medication is prescribed by or in consultation with an oncologist.

27. Thymic Carcinoma. Approve for 1 year if the patient meets BOTH of the following (A and B):
A) Patient is ≥ 18 years of age; AND
B) The medication is prescribed by or in consultation with an oncologist.

28. Vulvar Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):
A) Patient is ≥ 18 years of age; AND
B) Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.
C) Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); AND
Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
D) The tumor is PD-L1-positive (combined positive score ≥ 1), as determined by an approved test; AND
E) Patient has tried at least one other chemotherapy regimen; AND

Note: Examples of chemotherapy regimen are cisplatin, carboplatin, fluorouracil, paclitaxel.

F) The medication is prescribed by or in consultation with an oncologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Keytruda is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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