Generic Name: Pembrolizumab

Therapeutic Class or Brand Name: Keytruda®

Applicable Drugs (if Therapeutic Class): N/A

Preferred: N/A

Non-preferred: N/A

Date of Origin: 4/19/2017

Date Last Reviewed / Revised: 8/16/2023

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through V are met)

I. Documented diagnosis of one of the following conditions A through R AND must meet criteria listed under applicable diagnosis:

A. Melanoma:

1. Unresectable or metastatic melanoma and criterion a is met:
   a) Keytruda® will be used as a single agent.
2. Stage IIB, IIC, or III melanoma following complete resection and criterion a is met:
   a) Keytruda® will used for the adjuvant treatment of adult and pediatric (12 years and older).

B. Non-small cell lung cancer (NSCLC):

1. Combination therapy with either "a" or "b" and criteria under each is met:
   a) Metastatic non-squamous NSCLC undergoing first-line treatment and criteria 1 and 2 are met:
      (1) EGFR or ALK genomic tumor aberrations are not present.
      (2) Keytruda® will be used in combination with pemetrexed and platinum chemotherapy.
   b) Metastatic squamous NSCLC undergoing first-line treatment and criteria 1 is met:
      (1) Keytruda® will be used in combination with carboplatin and either paclitaxel or paclitaxel protein-bound.
2. Monotherapy either "a", "b" or "c"and the criteria under each is met:
   a) NSCLC tumor expresses PD-L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test and the following criteria 1 through 3 are met:
      (1) EGFR or ALK genomic tumor aberrations are not present.
      (2) Disease is stage III and patient is not a candidate for surgical resection or definitive chemoradiation OR is disease is metastatic

(3) Keytruda® will be used as a single agent.

b) Metastatic NSCLC tumor expresses PD-L1 (TPS ≥1%) as determined by an FDA-approved test the following criteria 1 through 3 are met:

(1) Has disease progression on or after platinum-containing chemotherapy.

(2) EGFR or ALK genomic tumor aberrations are present and patient has received FDA approved treatment for aberrations.

(3) Keytruda® will be used as a single agent.

c) Stage IB (T2a ≥4 cm), II, or IIIA NSCLC and criteria 1 and 2 are met:

(1) Keytruda® will used for the adjuvant treatment following resection and platinum-based chemotherapy.

(2) Keytruda® will be used as a single agent.

C. Metastatic head and neck squamous cell carcinoma (HNSCC) and ONE of the following criteria are met:

1. Metastatic, unresectable, or recurrent HNSCC
   a) Keytruda® will be used in combination with platinum and fluorouracil.
2. Metastatic, unresectable, or recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA approved test.
   a) Keytruda® will be used as a single agent.
3. Documentation of disease progression on or after platinum-containing chemotherapy.
   a) Keytruda® will be used as a single agent.

D. Refractory classical Hodgkin lymphoma (cHL) Monotherapy either "a" or "b" and the criteria under each is met:

a) Adult patients:

(1) Documentation that disease has relapsed.

(2) Keytruda® will be used as a single agent.

b) Pediatric patients:

(1) Documentation that disease has relapsed after 2 or more lines of therapy.

(2) Keytruda® will be used as a single agent.

E. Primary Mediastinal Large B-Cell Lymphoma (PMBCL) with refractory disease in adult and pediatric patients and criteria 1 through 3 are met:

1. Documentation of relapse after 2 or more prior lines of therapy
2. Documentation patient did not receive urgent cytoreductive therapy.

3. Keytruda® will be used as a single agent.

F. Urothelial carcinoma, locally advanced or metastatic disease and one of the following criteria are met:
   1. Patients is not eligible for any platinum-containing chemotherapy and criteria a is met:
      a) Keytruda® will be used as a single agent.
   2. Patient has disease progression and criteria a and b are met:
      a) Disease progression was during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
      b) Keytruda® will be used as a single agent.
   3. 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.
      a) Keytruda® will be used as a single agent.
   4. Patient is not eligible for cisplatin-containing chemotherapy and criteria a is met.
      a) Keytruda will be used in combination with enfortumab vedotin.

G. Unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient solid tumors and criteria 1 and 2 are met:
   1. If the patient has solid tumors, documentation of disease progression following prior treatment and that patient has no satisfactory alternative treatment options.
   2. Keytruda® will be used as a single agent.

H. Unresectable or metastatic Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer (CRC) and criteria 1 and 2 are met:
   1. Documentation the Keytruda® will be used as first line treatment.
   2. Keytruda® will be used as a single agent.

I. Locally Advanced or metastatic gastric or gastroesophageal junction adenocarcinoma when the following criteria is met:
   1. Locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma and criteria a is met:
      a) Keytruda will be used in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy.

J. Locally advanced, or metastatic esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma when the following criteria are met:
   1. Documentation that disease is not amenable to surgical resection or definitive chemoradiation and either "a" or "b" and the criteria under each is met:
      a) Documentation the tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA-approved test.
         (1) Keytruda® will be used as a single agent.
      b) Keytruda® will be used in combination with platinum- and fluoropyrimidine-based chemotherapy.

K. Recurrent or metastatic cervical cancer and criteria 1 or 2 and criteria under each is met:
   1. Documentation of disease progression on or after chemotherapy whose tumors express PD-L1[Combined Positive Score (CPS) ≥ 1] as determined by an FDA approved test.
      a) Keytruda® will be used as a single agent.
   2. Patients with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.
      a) Keytruda® will be used in combination with chemotherapy, with or without bevacizumab.

L. Hepatocellular Carcinoma (HCC)and the following criteria 1 through 2 are met:
   1. Documentation of previous treatment with sorafenib.
   2. Keytruda® will be used as a single agent.

M. Recurrent locally advanced or metastatic Merkel Cell Carcinoma (MCC) in adults and pediatric patients and the following criteria is met:
   1. Keytruda® will be used as a single agent.

N. Renal Cell Carcinoma (RCC) and one of the following criteria is met:
   1. Keytruda® will be used as first line treatment with Inlyta® (axitinib) or Lenvima® (lenvatinib).
   2. Keytruda® will be used as adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions

O. Endometrial carcinoma and criteria 1 or 2 and criteria under each is met:

1. The patient has advanced endometrial carcinoma that is mismatch repair proficient (pMMR) or it is not MSI-H and criteria a through c are met:
    a) Documentation of disease progression following prior systemic therapy.
    b) Patient is not a candidate for curative surgery or radiation.
    c) Keytruda® will be used in combination with Lenvima™(lenvatinib).
2. The patient has advanced endometrial carcinoma that is MSI-H or dMMR and criteria a and b are met:
    a) Documentation of disease progression following prior systemic therapy.
    b) Patient is not a candidate for curative surgery or radiation.
    c) Keytruda® will be used as a single agent.

P. Unresectable or metastatic tumor mutational burden high (TMB-H) in adult and pediatric patients and the following criteria are met:
    a) Documentation of disease progression on or after chemotherapy whose tumors express [≥10 mutations/megabase (mut/Mb) as determined by an FDA-approved test.
    b) Alternative treatment options are not available.
    c) Keytruda® will be used as a single agent.

Q. Recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC and criteria 1 and 2 are met:
    1. Documentation disease is not curable by surgery or radiation.
    2. Keytruda® will be used as a single agent.

R. Triple-Negative Breast Cancer and criteria 1 or 2 and criteria under each is met:
    1. Recurrent unresectable or metastatic triple negative breast cancer (TNBC) and criteria a and b are met:
        a) Documentation that tumor has expression of PD-L1[Combined Positive Score (CPS) ≥ 10] as determined by and FDA approved test.
        b) Keytruda® will be used in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery
    2. Locally recurrent, unresectable or metastatic triple negative breast cancer (TNBC) and criteria a and b are met:

a) Documentation that tumor has expression of PD-L1[Combined Positive Score (CPS) ≥ 10] as determined by and FDA approved test.

b) Keytruda® will be used in combination with chemotherapy.

II. Minimum age requirement: 2 years old.

III. Treatment is prescribed by or in consultation with an oncologist or a hematologist.

IV. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

V. Refer to plan document for the list of preferred products. If requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- Prior treatment with a programmed death receptor-1 (PD-1)-blocking antibody or a programmed death-ligand 1 (PD-L1) blocking antibody (i.e. Bavencio®, Imfinzi™, Keytruda®, Opdivo®, or Tecentriq®).

OTHER CRITERIA

- N/A

QUANTITY / DAYS SUPPLY RESTRICTIONS

Monotherapy

Adult dosing as monotherapy

- Melanoma unresectable or metastatic
  - 200 mg every 3 weeks OR 400 mg every 6 weeks until disease progression or unacceptable toxicity
- Melanoma adjuvant treatment
  - 200 mg every 3 weeks OR 400 mg every 6 weeks up to 12 months
- NSCLC, SCLC, HNSCC, cHL, PMBCL, Urothelial carcinoma, MSI-H or dMMR cancer, MSI-H or dMMR CRC, Gastric Cancer, Esophageal Cancer, Cervical Cancer, HCC, MCC, TMB-H Cancer or cSCC, RCC, Endometrial Carcinoma, TNCB, BCG-unresponsive NMIBC
  - 200 mg every 3 weeks OR 400 mg every 6 weeks up 24 months.

Pediatric dosing:

- cHL, PMBCL, MSI-H Cancer, MCC, TMB-H Cancer

- Pediatrics: 2mg/kg (up to 200 mg) every 3 weeks x 24 months.

APPROVAL LENGTH

- **Authorization:** 6 months
- **Re-Authorization:** An updated letter of medical necessity or progress notes showing that current medical necessity criteria are met and that the medication is effective. *Please note:* For all diagnoses except for melanoma as noted above, Keytruda® is only indicated to be given for up to a total of 24 months

APPENDIX

N/A

REFERENCES

1. Keytruda. Prescribing information. Merck & Co Inc.; 2023. Accessed August, 2023. http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf.
2. NCCN Clinical Practice Guidelines in Oncology. Melanoma: Cutaneous V.3.2022. Updated April 11, 2022. Accessed October 19, 2022. https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf.
3. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell lung Cancer V.5.2022. Updated September 26, 2022. Accessed October 19, 2022. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
4. NCCN Clinical Practice Guidelines in Oncology. Head and Neck cancers V.2.2022. Updated April 26, 2022. Accessed October 19, 2022. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf.
5. NCCN Clinical Practice Guidelines in Oncology. Esophageal and Esophagastric junction cancers V.4.2022. Updated September 7, 2022. Accessed October 19, 2022. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf.
6. NCCN Clinical Practice Guidelines in Oncology. breast Cancer V.4.2022. Updated June 21, 201. Accessed October 19, 2022. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
7. NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer V.3.2023. Updated September 22, 2022. Accessed October 19, 2022. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.

DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.