BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.21.50

Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Antineoplastic Agents	**Original Policy Date:**	September 26, 2014
Subject:	Keytruda	**Page:**	1 of 15

Last Review Date: June 16, 2022

Keytruda

Description

Keytruda (pembrolizumab)

Background
Keytruda (pembrolizumab) is a monoclonal antibody for the treatment of patients with many different types of cancer. Keytruda blocks a cellular pathway known as PD-1, human programmed death receptor-1, which restricts the body's immune system from attacking cancer cells (1-2).

Regulatory Status
FDA-approved indications: Keytruda is a human programmed death receptor-1 (PD-1)-blocking antibody indicated: (1)

1. Melanoma
    a. For the treatment of patients with unresectable or metastatic melanoma
    b. For the adjuvant treatment of adult and pediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma following complete resection
2. Non-Small Cell Lung Cancer (NSCLC)
    a. In combination with pemetrexed and platinum chemotherapy, as first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations
    b. In combination with carboplatin and either paclitaxel or paclitaxel protein-bound, as first-line treatment of patients with metastatic squamous NSCLC
    c. 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:

i. Stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
ii. Metastatic.

d. 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.

3. Head and Neck Squamous Cell Cancer (HNSCC)
   a. In combination with platinum and fluorouracil (FU), for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC.
   b. 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.
   c. As a single agent, for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.
4. Classical Hodgkin Lymphoma (cHL)
   a. For the treatment of adult patients with relapsed or refractory cHL
   b. For the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy
5. Primary Mediastinal Large B-Cell Lymphoma (PMBCL)
   a. For the treatment of adult and pediatric patients with refractory PMBCL, or who have relapsed after 2 or more prior lines of therapy
   b. Limitations of Use: Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.
6. Urothelial Carcinoma
   a. For the treatment of patients with locally advanced or metastatic urothelial carcinoma:
      i. who are not eligible for any platinum-containing chemotherapy, or
      ii. who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
   b. 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
7. Microsatellite Instability-High or Mismatch Repair Deficient Cancer
   a. For the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid

tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options

b. Limitations of Use: The safety and effectiveness of Keytruda in pediatric patients with MSI-H central nervous system cancers have not been established.

8. Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer (CRC)
   a. For the treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC)
9. Gastric Cancer
   a. In combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma
10. Esophageal Cancer
    a. For the treatment of patients with recurrent 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:
       i. In combination with platinum- and fluoropyrimidine-based chemotherapy, or
       ii. 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
11. Cervical Cancer
    a. 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
    b. 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 (CPS ≥1) as determined by an FDA-approved test
12. Hepatocellular Carcinoma (HCC)
    a. For the treatment of patients with HCC who have been previously treated with sorafenib
13. Merkel Cell Carcinoma (MCC)
    a. For the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma
14. Renal Cell Carcinoma (RCC)
    a. In combination with axitinib, for the first-line treatment of patients with advanced RCC

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

15. Endometrial carcinoma
    a. In combination with lenvatinib, for the treatment of patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation
    b. As a single agent, for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by and FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation
16. Tumor Mutational Burden-High (TMB-H) Cancer
    a. 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
    b. Limitations of Use: The safety and effectiveness of Keytruda in pediatric patients with TMB-H central nervous system cancers have not been established.
17. Cutaneous Squamous Cell Carcinoma (cSCC)
    a. For the treatment of patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC that is not curable by surgery or radiation
18. Triple-Negative Breast Cancer (TNBC)
    a. For treatment of patients with high-risk early-stage TNBC in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery
    b. 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
19. Adult Indications: Additional Dosing Regimen of 400 mg every 6 weeks
    a. For use at an additional recommended dosage of 400 mg every 6 weeks for all approved adult indications

Clinically significant immune-mediated adverse reactions may occur with Keytruda therapy including pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hyperthyroidism, hypothyroidism, skin adverse reactions, infusion-related reactions, and other immune-mediated adverse

reactions. Based on the severity of the adverse reaction, Keytruda should be withheld or discontinued and corticosteroids administered. Patients should be monitored for signs and symptoms of pneumonitis, colitis, hypophysitis, thyroid disorders, and changes in liver and renal function. Keytruda may cause fetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised of the potential hazard to a fetus (1).

Keytruda in combination with axitinib can cause hepatic toxicity with higher than expected frequencies of Grades 3 and 4 ALT and AST elevations compared to Keytruda alone (1).

The safety and effectiveness of Keytruda have been established in pediatric patients (1).

Related Policies
Bavencio, Jemperli, Opdivo, Opdualag, Tecentriq

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Keytruda may be considered **medically necessary** in patients with melanoma, non-small cell lung cancer (NSCLC), head and neck squamous cell cancer (HNSCC), classical Hodgkin lymphoma (cHL), primary mediastinal large B-cell lymphoma (PMBCL), urothelial carcinoma, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS), microsatellite instability-high or mismatch repair deficient cancers, gastric cancer, esophageal cancer, cervical cancer, hepatocellular carcinoma (HCC), Merkel cell carcinoma (MCC), renal cell carcinoma (RCC), endometrial carcinoma, tumor mutation burden-high (TMB-H) cancer, cutaneous squamous cell carcinoma (cSCC), or triple-negative breast cancer (TNBC); and if the conditions indicated below are met.

Keytruda may be considered **investigational** in patients with all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Unresectable or metastatic melanoma

2. Stage IIB, IIC, or III melanoma following complete resection
    a. Used as adjuvant treatment

3. Metastatic non-small cell lung cancer (NSCLC)
    a. Used as a single agent
    b. PD-L1 tumor expression with Tumor Proportion Score (TPS) ≥ 1% determined by an FDA-approved test with **ONE** of the following:
        i. Negative for EGFR or ALK tumor expression and **ONE** of the following:
            i. Disease progression on or after platinum-containing chemotherapy
            ii. First-line treatment
        ii. Positive EGFR or ALK tumor expression
            1) Disease progression after targeted FDA-approved therapy

4. Metastatic nonsquamous non-small cell lung cancer (NSCLC)
    a. Used in combination with pemetrexed and platinum chemotherapy as first-line treatment
    b. Negative for EGFR or ALK tumor expression

5. Stage III non-small cell lung cancer (NSCLC)
    a. Patient is not a candidate for surgical resection or definitive chemoradiation
    b. PD-L1 tumor expression with Tumor Proportion Score (TPS) ≥ 1% as determined by an FDA-approved test
    c. Negative for EGFR or ALK tumor aberrations
    d. Used as a single agent for first-line treatment

6. Metastatic squamous non-small cell lung cancer (NSCLC)
    a. Used in combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment

7. Recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) and **ONE** of the following:
    a. Used in combination with platinum and fluorouracil (FU) as first-line treatment
    b. PD-L1 tumor expression with combined positive score (CPS) ≥ 1 as determined by an FDA-approved test
        i. Used as a single agent for first-line treatment
    c. Disease progression on or after platinum-containing chemotherapy
        i. Used as a single agent

8. Classical Hodgkin lymphoma (cHL) with **ONE** of the following:
    a. Refractory cHL
    b. Relapsed cHL
        i. Age < 18 **only**: patient has relapsed after 2 or more prior lines of therapy

9. Refractory primary mediastinal large B-cell lymphoma (PMBCL)
    a. Patient has relapsed after 2 or more lines of therapy

10. Locally advanced or metastatic urothelial carcinoma with **ONE** of the following:
    a. Patient is **NOT** eligible for any platinum-containing chemotherapy
    b. Disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

11. Non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS)
    a. Bacillus Calmette-Guerin (BCG)-unresponsive
    b. Patient is considered high-risk
    c. Patient is ineligible for or has elected not to undergo cystectomy

12. Unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors
    a. Solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options
    b. **NOT** for use in pediatric patients with MSI-H central nervous system cancers
    c. Diagnosis has been confirmed by polymerase chain reaction (PCR) or immunohistochemistry (IHC) test

13. Unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC)
    a. Diagnosis has been confirmed by polymerase chain reaction (PCR) or immunohistochemistry (IHC) test

14. Locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma
    a. Used in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy
    b. Used as first-line treatment

15. Locally advanced or metastatic esophageal or gastroesophageal junction carcinoma
    a. Carcinoma is not amenable to surgical resection or definitive chemoradiation
    b. Keytruda is being used as **ONE** of the following:
        i. In combination with platinum- and fluoropyrimidine-based chemotherapy
        ii. 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

16. Cervical cancer
    a. Patient has **ONE** of the following:
        a. Persistent, recurrent, or metastatic cervical cancer
            i. Used in combination with chemotherapy
        b. Recurrent or metastatic cervical cancer
            i. Used as a single agent
            ii. Disease progression on or after chemotherapy
    b. PD-L1 tumor expression with combined positive score (CPS) ≥ 1 as determined by an FDA-approved test

17. Hepatocellular carcinoma (HCC)
    a. Patient has previously been treated with Nexavar (sorafenib)

18. Recurrent locally advanced or metastatic Merkel cell carcinoma (MCC)

19. Advanced renal cell carcinoma (RCC) **AND ONE** of the following:
    a. First-line treatment
        i. Used in combination with Inlyta (axitinib) **OR** Lenvima (lenvatinib)
        ii. Prescriber agrees to monitor for hepatotoxicity
    b. Adjuvant treatment in patients with **ONE** of the following:
        i. Intermediate-high or high risk of recurrence following nephrectomy
        ii. Following nephrectomy and resection of metastatic lesions

20. Advanced endometrial carcinoma
    a. Patient has **ONE** of the following:
        i. MSI-H or dMMR, as determined by an FDA-approved test
            1. Used as a single agent

ii. **NOT** MSI-H or dMMR
1. Used in combination with Lenvima (lenvatinib)

b. Disease progression following prior systemic therapy
c. **NOT** a candidate for curative surgery or radiation

21. Unresectable or metastatic tumor mutational burden-high (TMB-H) solid tumors
    a. ≥10 mutations/megabase (mut/Mb) as determined by an FDA-approved test
    b. Disease has progressed following prior treatment
    c. Patient has no satisfactory alternative treatment options
    d. **NOT** for use in pediatric patients with TMB-H central nervous system cancers

22. Recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC
    a. **NOT** curable by surgery or radiation

23. Triple-Negative Breast Cancer (TNBC) and **ONE** of the following:
    a. High-risk early-stage TNBC
        i. Used in combination with chemotherapy as neoadjuvant treatment **OR**
        ii. Used as a single agent after surgery as adjuvant treatment
    b. Locally recurrent unresectable or metastatic TNBC
        i. PD-L1 tumor expression with combined positive score (CPS) ≥ 10 as determined by an FDA-approved test
        ii. Used in combination with chemotherapy

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following:
1. Unresectable or metastatic melanoma
2. Stage IIB, IIC, or III melanoma following complete resection
3. Metastatic non-small cell lung cancer (NSCLC)
4. Metastatic nonsquamous non-small cell lung cancer (NSCLC)
5. Stage III non-small cell lung cancer (NSCLC)
6. Metastatic squamous non-small cell lung cancer (NSCLC)
7. Recurrent or metastatic head and neck squamous cell carcinoma (HNSCC)

8. Relapsed or refractory classical Hodgkin lymphoma (cHL)
9. Refractory primary mediastinal large B-cell lymphoma (PMBCL)
10. Locally advanced or metastatic urothelial carcinoma
11. Non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS)
12. Unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors
    a. **NOT** for use in pediatric patients with MSI-H central nervous system cancers
13. Unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer
14. Locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma
    a. Used in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy
15. Locally advanced or metastatic esophageal or gastroesophageal junction carcinoma
16. Persistent, recurrent, or metastatic cervical cancer
17. Hepatocellular carcinoma (HCC)
18. Recurrent locally advanced or metastatic Merkel cell carcinoma (MCC)
19. Advanced renal cell carcinoma (RCC) **AND ONE** of the following:
    a. First-line treatment
        i. Used in combination with Inlyta (axitinib) **OR** Lenvima (lenvatinib)
        ii. Prescriber agrees to monitor for hepatotoxicity
    b. Adjuvant treatment
20. Advanced endometrial carcinoma
    a. Used as a single agent **OR** used in combination with Lenvima (lenvatinib)
21. Unresectable or metastatic tumor mutational burden-high (TMB-H) solid tumors
    a. **NOT** for use in pediatric patients with TMB-H central nervous system cancers
22. Recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC
23. Triple-negative breast cancer (TNBC) and **ONE** of the following:
    a. High-risk early-stage TNBC used as single agent as adjuvant treatment
    b. Locally recurrent unresectable or metastatic TNBC used in combination with chemotherapy

AND the following:

a. Prescriber agrees to discontinue treatment for any immune mediated adverse reaction (encephalitis, nephritis, rash, decreased renal function and endocrinopathies) or disease progression

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits
Same as above

Rationale

Summary
Keytruda (pembrolizumab) is a monoclonal antibody indicated for the treatment of patients with many different types of cancer. Clinically significant immune-mediated adverse reactions may occur with Keytruda therapy including pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hyperthyroidism, hypothyroidism, skin adverse reaction, infusion-related reactions, and other immune-mediated adverse reactions. Based on the severity of the adverse reaction, Keytruda should be withheld or discontinued, and corticosteroids administered. Keytruda may cause fetal harm when administered to a pregnant woman. The safety and effectiveness of Keytruda have been established in pediatric patients (1-2).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Keytruda while maintaining optimal therapeutic outcomes.

References
1. Keytruda [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; March 2022.
2. NCCN Drugs & Biologics Compendium® Pembrolizumab 2022. National Comprehensive Cancer Network, Inc. Accessed on May 3, 2022.

Policy History

Date	Action
September 2014	New Policy
December 2014	Annual editorial review and reference update

June 2015	Annual editorial review
October 2015	Addition of Metastatic non-small cell lung cancer (NSCLC) if the patient has PD-L1 tumor expression determined by a FDA-approved test and has disease progression on or after platinum-containing chemotherapy; or the patient has EGFR or ALK tumor expression and has disease progression after FDA-approved therapy
December 2015	Annual review Removal of disease progression following Yervoy (ipilimumab) and, if BRAF V600 mutation positive, a BRAF inhibitor and no concurrent therapy with other agents for the treatment of unresectable or metastatic melanoma
March 2016	Annual editorial review Policy number change from 5.04.50 to 5.21.50
June 2016	Annual editorial review Addition of Prescriber agrees to discontinue treatment for any immune mediated adverse reaction (encephalitis, nephritis, rash, decreased renal function and endocrinopathies) or disease progression in renewal section per SME
August 2016	Addition of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy
September 2016	Annual review
November 2016	Addition of (NSCLC) PD-L1 tumor expression with Tumor Proportion Score (TPS) ≥ 50% determined by a FDA-approved test with no prior treatment needed
December 2016	Annual review
March 2017	Addition of refractory classical Hodgkin lymphoma (cHL), who have relapsed after 3 or more prior lines of therapy Removal of the age requirement
June 2017	Annual editorial review and reference update Addition of metastatic nonsquamous non-small cell lung cancer (NSCLC) Addition of advanced or metastatic urothelial carcinoma Addition of Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancers with additional requirements to criteria
July 2017	Addition of the requirement to MSI-H: diagnosis has to be confirmed by PCR-based genetic testing
September 2017	Annual review
October 2017	Addition of recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma
December 2017	Annual review
June 2018	Annual editorial review and reference update

July 2018	Addition of the diagnosis of recurrent or metastatic cervical cancer Addition of use of medication in patients with locally advanced or metastatic urothelial carcinoma in patients who are not eligible for any platinum-containing chemotherapy
August 2018	Addition of diagnosis of refractory primary mediastinal large B-cell lymphoma (PMBCL) Addition of no EGFR or ALK genomic tumor aberrations requirement to metastatic nonsquamous NSCLC
September 2018	Annual editorial review and reference update
November 2018	Annual review and reference update. Addition of indication of metastatic squamous NSCLC. Change NSCLC indication with pemetrexed and platinum chemotherapy. Addition to warnings. Addition of hepatocellular carcinoma indication
January 2019	Addition of indication: recurrent locally advanced or metastatic Merkel cell carcinoma (MCC)
March 2019	Annual review and reference update. Addition of indication of melanoma with involvement of lymph node(s) following complete resection as adjuvant treatment
April 2019	Addition of indication: Stage III NSCLC Addition of indication: Advanced renal cell carcinoma (RCC)
May 2019	Revised Metastatic NSCLC indication to include first-line therapy with TPS ≥1% and negative for EGFR or ALK tumor expression. Added hepatotoxicity monitoring requirement to RCC diagnosis
June 2019	Annual review. Added HNSCC indication used in combination with platinum and fluorouracil as first-line treatment and HNSCC as a single agent for first-line treatment with CPS >1. Added small cell lung cancer indication
August 2019	Addition of indication: Recurrent locally advanced or metastatic squamous cell carcinoma of the esophagus. Revised Metastatic NSCLC indication
September 2019	Annual review. Addition of indication: endometrial carcinoma
January 2020	Addition of indication: Non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS). Changed initial approval duration to 12 months
March 2020	Annual review and reference update
July 2020	Addition of indications: Tumor mutational burden-high (TMB-H) solid tumors; adult indications: additional dosing regimen of 400 mg every 6 weeks; and recurrent or metastatic cutaneous squamous cell carcinoma (cSCC). Addition of indication: first-line treatment for unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC). Revised testing for MSI-H and dMMR cancers to “Diagnosis has been confirmed by

	polymerase chain reaction (PCR) or immunohistochemistry (IHC) test". Revised continuation requirement that "NOT for use in MSI CNS cancers in pediatric patients" only applies to patients with solid tumors
September 2020	Annual review
October 2020	Revised cHL indication to relapsed or refractory cHL and pediatric patients with relapsed cHL must have relapsed after 2 or more lines of therapy
November 2020	Addition of indication: triple-negative breast cancer (TNBC)
December 2020	Annual review
April 2021	Revised indication per package insert: locally advanced or metastatic esophageal or gastroesophageal junction carcinoma
May 2021	Removed small cell lung cancer (SCLC) indication per latest package insert update. Addition of indication: locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma
June 2021	Annual review
July 2021	Removed requirements from MSI-H or dMMR colorectal cancer stating that Keytruda needs to be used as first-line treatment or after disease progression on fluoropyrimidine, oxaliplatin, and irinotecan. Addition of indication: locally advanced cutaneous squamous cell carcinoma. Revised Triple-Negative Breast Cancer (TNBC) indication to include patients with high-risk early stage TNBC
September 2021	Annual review. Added option to use in combination with Lenvima in advanced RCC. Removed requirement for PD-L1 CPS score for locally advanced or metastatic urothelial carcinoma.
November 2021	Added indication of persistent, recurrent, or metastatic cervical cancer used in combination with chemotherapy. Added "used as a single agent" to recurrent or metastatic cervical cancer with disease progression on or after chemotherapy
December 2021	Annual review. Added indication of adjuvant treatment of RCC in patients at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions
January 2022	Revised indication for adjuvant treatment of melanoma: no longer needs lymph node involvement and now requires Stage IIB, IIC, or III melanoma
March 2022	Annual editorial review and reference update. Per package insert update: Removed third line gastric cancer indication, i.e., "Keytruda, as a single agent, for the treatment of patients with recurrent locally advanced or metastatic gastric or GEJ adenocarcinoma whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test, with disease progression on or after 2 or more prior lines of therapy including

	fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu targeted therapy"
April 2022	Addition of indication per PI update: advanced endometrial carcinoma that is MSI-H or dMMR
June 2022	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.