

SPECIALTY GUIDELINE MANAGEMENT

KEYTRUDA (pembrolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Melanoma
Keytruda is indicated for the treatment of patients with unresectable or metastatic melanoma.
2. Non-Small Cell Lung Cancer
 - i. Keytruda, as a single agent, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) $\geq 50\%$] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.
 - ii. Keytruda, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS $\geq 1\%$) 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.
 - iii. Keytruda, in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC.
3. Head and Neck Cancer
Keytruda is indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy.
4. Classical Hodgkin Lymphoma
Keytruda is indicated for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after three or more prior lines of therapy.
5. Urothelial Carcinoma
Keytruda is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:
 - i. Are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 10], or
 - ii. Are not eligible for platinum-containing chemotherapy, or
 - iii. Have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
6. Microsatellite Instability-High Cancer
Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient

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- i. Solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
- ii. Colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

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

7. Gastric Carcinoma

Keytruda is indicated for the treatment of patients with recurrent, locally advanced, metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) \geq 1] as determined by an FDA approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine and platinum containing chemotherapy and if appropriate, HER2/neu targeted therapy.

8. Cervical Cancer

Keytruda is indicated for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumor express PD-L1 [Combined Positive Score (CPS) \geq 1] as determined by an FDA approved test

9. Primary Mediastinal large B-cell Lymphoma (PMBCL)

Keytruda is indicated for the treatment of adult and pediatric patients with refractory PMBCL, or who have relapsed after 2 or more prior lines of therapy.

Limitation of Use: Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

B. Compendial Uses

1. Non-small cell lung cancer
2. Unresectable advanced or metastatic microsatellite instability-high colorectal cancer
3. Malignant pleural mesothelioma
4. Merkel cell carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for pediatric patients with microsatellite instability-high (MSI-H) central nervous system cancers.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma

Authorization of 12 months may be granted for treatment of unresectable or metastatic melanoma.

B. Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of metastatic NSCLC in either of the following settings:

1. First-line treatment

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- i. The tumor has high PD-L1 expression [Tumor Proportion Score (TPS) \geq 50%] and EGFR, ALK, or ROS1 genomic tumor markers are negative or unknown, OR
- ii. The patient has nonsquamous NSCLC and Keytruda will be used in combination with pemetrexed and carboplatin.
- 2. Subsequent therapy
 - i. The patient's tumor is positive for the PD-L1 protein, AND
 - ii. Keytruda is requested for disease progression on a first-line cytotoxic regimen or for further progression on other systemic therapy.

C. Head and Neck Cancer

Authorization of 12 months may be granted for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy.

D. Classical Hodgkin Lymphoma

Authorization of 12 months may be granted for treatment of refractory or relapsed classical Hodgkin lymphoma.

E. Urothelial carcinoma

Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial carcinoma when any of the following criteria is met:

- 1. Patient is not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combined Positive Score (CPS) \geq 10].
- 2. Patient is not eligible for platinum-containing chemotherapy.
- 3. Patient experienced disease progression during or following platinum-containing chemotherapy.
- 4. Patient experienced disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

F. Microsatellite Instability-High Cancer

Authorization of 12 months may be granted for treatment of unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient solid tumors when either of the following criteria are met:

- 1. The patient has colorectal cancer
- 2. For other solid tumors: Member experienced disease progression following prior treatment and has no satisfactory alternative treatment options.

G. Malignant Pleural Mesothelioma

Authorization 12 months may be granted for treatment of malignant pleural mesothelioma.

H. Merkel Cell Carcinoma

Authorization of 12 months may be granted for treatment of Merkel cell carcinoma.

I. Gastric Carcinoma

Authorization of 12 months may be granted for treatment of recurrent locally advanced, metastatic gastric or gastroesophageal junction adenocarcinoma when all of the following criteria are met:

- 1. Tumor expresses PD-L1 [Combined Positive Score (CPS) greater than equal to 1].
- 2. Patient experienced disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy.
- 3. If HER2 positive, patient received HER2/neu-targeted therapy.

J. Cervical Cancer

Reference number(s)
1889-A

Authorization of 12 months may be granted for the treatment of recurrent or metastatic cervical cancer when all of the following criteria are met:

1. Tumor expresses PD-L1 [Combined Positive Score (CPS) greater than equal to 1].
2. Patient has experienced disease progression on or after chemotherapy.

K. Primary Mediastinal Large B-Cell Lymphoma (PMBCL)

Authorization of 12 months may be granted for the treatment of patients with PMBCL who do not require urgent cytoreductive therapy when one of the following criteria is met:

1. Patient has refractory disease.
2. Patient has relapsed after 2 or more prior lines of therapy.

IV. CONTINUATION OF THERAPY

All patients (including new patients) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Keytruda [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; June 2018.
2. The NCCN Drugs & Biologics Compendium® © 2016 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 7, 2017.