

## 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
  - i. Keytruda (pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma.
  - ii. Keytruda is indicated for the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection.
2. Non-Small Cell Lung Cancer
  - i. Keytruda, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.
  - ii. Keytruda, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.
  - iii. Keytruda, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS)  $\geq 1\%$ ] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
    - a. stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
    - b. metastatic.
  - iv. 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.
3. Head and Neck Squamous Cell Cancer
  - i. Keytruda, in combination with platinum and fluorouracil (FU), is indicated for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC).
  - ii. Keytruda, as a single agent, is indicated for the first line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS)  $\geq 1$ ] as determined by an FDA-approved test.
  - iii. Keytruda, as a single agent, is indicated for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.
4. Classical Hodgkin Lymphoma
  - i. Keytruda is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL).

- ii. Keytruda is indicated for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more prior lines of therapy.
5. **Primary Mediastinal Large B-cell Lymphoma**  
Keytruda is indicated for the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma (PMBCL), or who have relapsed after 2 or more prior lines of therapy.
- Limitations of Use: Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.
6. **Urothelial Carcinoma**
- i. Keytruda is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (CPS  $\geq$  10) as determined by an FDA-approved test, or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.
  - ii. Keytruda is indicated for the 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.
  - iii. Keytruda is indicated 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 Cancer or Mismatch Repair Deficient 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 (dMMR)
- 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.
- 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)**  
Keytruda is indicated for the first-line treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC).
9. **Gastric Cancer**
- i. Keytruda is indicated as a single agent for the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 (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.
  - ii. Keytruda is indicated 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**  
Keytruda is indicated for the treatment of patients with 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:

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- 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 whose tumors express PD-L1 (CPS  $\geq$  10) as determined by an FDA-approved test.
11. **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 (CPS  $\geq$  1) as determined by an FDA-approved test.
  12. **Hepatocellular Carcinoma**  
Keytruda is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.
  13. **Merkel Cell Carcinoma**  
Keytruda is indicated for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC).
  14. **Renal Cell Carcinoma**  
Keytruda, in combination with axitinib, is indicated for the first-line treatment of patients with advanced renal cell carcinoma (RCC).
  15. **Endometrial Carcinoma**  
Keytruda, in combination with lenvatinib, is indicated for the treatment of patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.
  16. **Tumor Mutational Burden-High Cancer**  
Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [ $\geq$ 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.  
  
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**  
Keytruda is indicated for the treatment of patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) that is not curable by surgery or radiation.
  18. **Triple-Negative Breast Cancer**  
Keytruda is indicated in combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 [Combined Positive Score (CPS)  $\geq$ 10] as determined by an FDA approved test.

**B. Compendial Uses**

1. Cutaneous melanoma
2. Non-small cell lung cancer
3. Head and neck squamous cell cancer
4. Classical Hodgkin Lymphoma
5. Urothelial carcinoma

- i. Bladder cancer
- ii. Primary carcinoma of the urethra
- iii. Upper genitourinary tract tumors
- iv. Urothelial carcinoma of the prostate
6. Solid tumors
7. Adrenocortical carcinoma
8. Anaplastic thyroid carcinoma
9. Follicular, hürthle cell, or papillary thyroid carcinoma
10. Medullary thyroid carcinoma
11. Colorectal cancer
12. Small bowel adenocarcinoma, including advanced ampullary cancer
13. Malignant pleural mesothelioma
14. Gastric cancer
15. Esophageal cancer
16. Esophagogastric junction cancer
17. Cervical cancer
18. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
19. Uveal melanoma
20. Testicular cancer
21. Endometrial carcinoma
22. Anal carcinoma
23. Central Nervous System (CNS) brain metastases
24. Primary mediastinal large B-cell lymphoma
25. Pancreatic adenocarcinoma
26. Hepatobiliary cancers
27. Vulvar cancer
28. Renal cell carcinoma
29. Thymic carcinoma
30. Mycosis Fungoides/Sezary syndrome
31. Extranodal NK/T-cell lymphoma, nasal type
32. Gestational trophoblastic neoplasia
33. Poorly differentiated neuroendocrine carcinoma/large or small cell carcinoma
34. Soft tissue sarcomas: alveolar soft part sarcoma (ASPS), myxofibrosarcoma, undifferentiated pleomorphic sarcoma (UPS), cutaneous angiosarcoma, and undifferentiated sarcoma.
35. Occult primary cancer

All other indications are considered experimental/investigational and not medically necessary.

## II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Documentation of programmed death ligand 1 (PD-L1) tumor expression, where applicable.
- B. Documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.
- C. Documentation of laboratory report confirming high tumor mutational burden ( $\geq 10$  mutations/megabase), where applicable.
- D. Documentation of laboratory report confirming that the cancer cells are negative for the following receptors, where applicable:
  1. Human epidermal growth factor receptor 2 (HER2)
  2. Estrogen

3. Progesterone
- E. Documentation of laboratory report confirming HER2 status, where applicable.

### III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

- A. Pediatric members with MSI-H central nervous system cancers.
- B. Pediatric members with TMB-H central nervous system cancers.
- C. Members who have experienced disease progression while on programmed death receptor-1 (PD-1) or PD-L1 inhibitor therapy (other than when used as second-line or subsequent therapy for metastatic or unresectable melanoma in combination with ipilimumab following progression on single agent anti-PD-1 immunotherapy).

### IV. CRITERIA FOR INITIAL APPROVAL

#### A. Cutaneous Melanoma

Authorization of 6 months may be granted for treatment of cutaneous melanoma in any of the following settings:

1. For unresectable or metastatic disease as a single agent.
2. For unresectable or metastatic disease in combination with ipilimumab following disease progression on single-agent anti-PD-1 immunotherapy.
3. As adjuvant treatment following complete lymph node resection or complete resection of metastatic disease as a single agent.

#### B. Non-small Cell Lung Cancer (NSCLC)

Authorization of 6 months may be granted for treatment of NSCLC in any of the following settings:

1. Treatment of recurrent, advanced or metastatic nonsquamous NSCLC:
  - i. Keytruda will be used following EGFR or ALK therapy if EGFR or ALK positive, AND
  - ii. Keytruda will be used in combination with both of the following:
    - a. Pemetrexed
    - b. Carboplatin or cisplatin.
2. Treatment of recurrent, advanced or metastatic squamous NSCLC:
 

Keytruda will be used in combination with carboplatin and paclitaxel or paclitaxel protein-bound.
3. Treatment of recurrent, advanced or metastatic NSCLC expressing PD-L1 (TPS  $\geq$ 1%):
  - i. Keytruda will be used as a single agent, AND
  - ii. Keytruda will be used following EGFR or ALK therapy if EGFR or ALK positive.

#### C. Head and Neck Squamous Cell Cancer

Authorization of 6 months may be granted for treatment of members with very advanced head and neck squamous cell carcinoma (HNSCC) when any of the following criteria is met:

1. Keytruda will be used as a single agent for first-line treatment in members whose tumors express PD-L1 (CPS  $\geq$ 1).
2. Keytruda will be used as a single agent for subsequent therapy (regardless of PD-L1 status).
3. Keytruda will be used in combination with fluorouracil and either carboplatin or cisplatin (regardless of PD-L1 status).

#### D. Classical Hodgkin Lymphoma

Authorization of 6 months may be granted as a single agent for treatment of relapsed or refractory classical Hodgkin lymphoma.

**E. Urothelial Carcinoma – Bladder Cancer**

Authorization of 6 months may be granted as a single agent for treatment of bladder cancer when any of the following criteria is met:

1. Keytruda will be used as first-line therapy in cisplatin ineligible members whose tumors express PD-L1 (CPS  $\geq$  10), or in members who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression for any of the following:
  - i. Stage II or Stage IIIA disease, if tumor is present following reassessment of tumor status 2-3 months after primary treatment with concurrent chemoradiotherapy.
  - ii. Locally advanced or metastatic disease.
  - iii. Metastatic or local recurrence post-cystectomy.
  - iv. Muscle invasive local recurrence or persistent disease in a preserved bladder.
2. Keytruda will be used as subsequent therapy following platinum-containing chemotherapy for any of the following:
  - i. Locally advanced or metastatic disease.
  - ii. Metastatic or local recurrence post-cystectomy.
  - iii. Muscle invasive local recurrence or persistent disease in a preserved bladder.
3. Keytruda will be used as subsequent therapy for the treatment of members with high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) when both of the following criteria are met:
  - i. Disease is Bacillus Calmette-Guerin (BCG)-unresponsive.
  - ii. Member is ineligible for or has elected not to undergo cystectomy.

**F. Urothelial Carcinoma – Primary Carcinoma of the Urethra**

Authorization of 6 months may be granted as a single agent for treatment of primary carcinoma of the urethra when either of the following criteria is met:

1. Keytruda will be used as first-line therapy for recurrent, locally advanced, or metastatic disease in cisplatin ineligible members whose tumors express PD-L1 (CPS  $\geq$  10), or in members who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression.
2. Keytruda will be used as subsequent therapy for recurrent, locally advanced or metastatic disease following platinum-containing chemotherapy.

**G. Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate**

Authorization of 6 months may be granted as a single agent for treatment of upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate when either of the following criteria is met:

1. Keytruda will be used as first-line therapy for locally advanced or metastatic disease in cisplatin ineligible members whose tumors express PD-L1 (CPS  $\geq$  10), or in members who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression.
2. Keytruda will be used as subsequent therapy for locally advanced or metastatic disease following platinum-containing chemotherapy.

**H. Solid Tumors**

Authorization of 6 months may be granted as a single agent for treatment of solid tumors in members with unresectable or metastatic disease that has progressed following prior treatment and who have no satisfactory alternative treatment options when either of the following criteria is met:

1. Keytruda will be used for microsatellite instability-high or mismatch repair deficient solid tumors.
2. Keytruda will be used for tumor mutational burden-high ( $\geq$ 10 mutations/megabase) solid tumors.

**I. Adrenocortical Carcinoma**

Authorization of 6 months may be granted for treatment of metastatic adrenocortical carcinoma.

**J. Anaplastic Thyroid Carcinoma**

Authorization of 6 months may be granted as a single agent for treatment of metastatic anaplastic thyroid carcinoma for tumor mutational burden-high ( $\geq 10$  mutations/megabase) tumors.

**K. Follicular, Hürthle Cell, or Papillary Thyroid Carcinoma**

Authorization of 6 months may be granted for treatment of unresectable or metastatic follicular, hürthle cell, or papillary thyroid carcinoma for tumor mutational burden-high ( $\geq 10$  mutations/megabase) tumors not amenable to radioactive iodine therapy.

**L. Medullary Thyroid Carcinoma**

Authorization of 6 months may be granted for treatment of unresectable, recurrent, or metastatic medullary thyroid carcinoma for tumor mutational burden-high ( $\geq 10$  mutations/megabase) tumors.

**M. Colorectal Cancer**

Authorization of 6 months may be granted as a single agent for the treatment of unresectable, advanced, or metastatic colorectal cancer, including appendiceal carcinoma, for microsatellite instability-high or mismatch repair deficient tumors.

**N. Small Bowel Adenocarcinoma**

Authorization of 6 months may be granted for treatment of advanced or metastatic small bowel adenocarcinoma, including advanced ampullary cancer, for microsatellite instability-high or mismatch repair deficient tumors.

**O. Malignant Pleural Mesothelioma**

Authorization 6 months may be granted as a single agent for subsequent treatment of malignant pleural mesothelioma.

**P. Merkel Cell Carcinoma**

Authorization of 6 months may be granted for treatment of Merkel cell carcinoma in members with recurrent locally advanced or metastatic disease.

**Q. Gastric Cancer**

Authorization of 6 months may be granted for treatment of gastric cancer in members who are not surgical candidates or have locally advanced, recurrent, or metastatic disease when any of the following criteria are met:

1. Keytruda will be used as second-line or subsequent therapy as a single agent for a tumor with microsatellite instability-high or deficient mismatch repair
2. Keytruda will be used as third-line or subsequent therapy as a single agent for a PD-L1 positive tumor (CPS  $\geq 1$ ).
3. Keytruda will be used as first-line therapy in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy for HER2-positive adenocarcinoma.

**R. Esophageal Cancer**

Authorization of 6 months may be granted for treatment of esophageal cancer in members who are not surgical candidates or have locally advanced, recurrent, or metastatic disease when any of the following conditions are met:

1. Keytruda will be used as second-line or subsequent therapy as a single agent for a tumor with microsatellite instability-high or deficient mismatch repair.
2. Keytruda will be used as second-line or subsequent therapy with PD-L1 tumor expression by CPS  $\geq 10$  for squamous cell carcinoma.
3. Keytruda will be used as third-line or subsequent therapy as a single agent with PD-L1 tumor expression by CPS  $\geq 1$ .
4. Keytruda will be used in combination with platinum and fluoropyrimidine-based chemotherapy.

**S. Esophagogastric Junction Cancer**

Authorization of 6 months may be granted for treatment of esophagogastric junction (EGJ) cancer, in members who are not surgical candidates or have locally advanced, recurrent, or metastatic disease when any of the following conditions are met:

1. Keytruda will be used as second-line or subsequent therapy as a single agent for a tumor with microsatellite instability-high or deficient mismatch repair.
2. Keytruda will be used as second-line or subsequent therapy with PD-L1 tumor expression by CPS  $\geq$  10 for squamous cell carcinoma.
3. Keytruda will be used as third-line or subsequent therapy as a single agent with PD-L1 tumor expression by CPS  $\geq$  1.
4. Keytruda will be used in combination with platinum and fluoropyrimidine-based chemotherapy.
5. Keytruda will be used as first-line therapy in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy for HER2-positive adenocarcinoma.

**T. Cervical Cancer**

Authorization of 6 months may be granted as a single agent for second-line therapy for the treatment of recurrent or metastatic cervical cancer when either of the following criteria is met:

1. Microsatellite instability-high or mismatch repair deficient tumors.
2. Member has experienced disease progression on or after chemotherapy for tumors that express PD-L1 (CPS  $\geq$  1).

**U. Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer**

Authorization of 6 months may be granted as a single agent for treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer for recurrent or persistent microsatellite instability-high or mismatch repair deficient tumors.

**V. Uveal Melanoma**

Authorization of 6 months may be granted as a single agent for treatment of uveal melanoma for distant metastatic disease.

**W. Testicular Cancer**

Authorization of 6 months may be granted as a single agent for third-line therapy for treatment of testicular cancer in members with microsatellite instability-high or mismatch repair deficient tumors.

**X. Endometrial Carcinoma**

Authorization of 6 months may be granted for treatment of endometrial carcinoma when the member meets either of the following criteria:

1. Keytruda will be used for recurrent, metastatic, or high-risk microsatellite instability-high or mismatch repair deficient tumors that have progressed following prior systemic therapy
2. Keytruda will be used in combination with lenvatinib for advanced endometrial carcinoma that is not microsatellite instability-high or mismatch repair deficient when the member has disease progression following prior systemic therapy and is not a candidate for curative surgery or radiation.

**Y. Anal Carcinoma**

Authorization of 6 months may be granted as a single agent for treatment of anal carcinoma for metastatic disease as second-line or subsequent therapy.

**Z. CNS Brain Metastases**

Authorization of 6 months may be granted as a single agent for treatment of CNS brain metastases in members with melanoma or PD-L1 positive non-small cell lung cancer.



**AA. Primary Mediastinal Large B-Cell Lymphoma**

Authorization of 6 months may be granted as a single agent for treatment of primary mediastinal large B-cell lymphoma in members with relapsed or refractory disease.

**BB. Pancreatic Adenocarcinoma**

Authorization of 6 months may be granted as a single agent for treatment of pancreatic adenocarcinoma in members with microsatellite instability-high or mismatch repair deficient tumors in any of the following settings:

1. Keytruda will be used as subsequent therapy for locally advanced or metastatic disease.
2. For local recurrence in the pancreatic operative bed after resection.
3. Keytruda will be used as first-line therapy for metastatic disease in members with poor performance status.

**CC. Hepatobiliary Cancers**

Authorization of 6 months may be granted as a single agent for treatment of unresectable or metastatic hepatobiliary cancers, including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer for disease that is microsatellite instability-high or mismatch repair deficient.

**DD. Hepatocellular Carcinoma**

Authorization of 6 months may be granted for treatment of members with hepatocellular carcinoma who have been previously treated with sorafenib.

**EE. Vulvar Cancer**

Authorization of 6 months may be granted as a single agent for second-line treatment of advanced, recurrent or metastatic disease in members with squamous cell vulvar cancer when either of the following criteria is met:

1. Member has microsatellite instability-high or mismatch repair deficient tumor.
2. Member has experienced disease progression on or after chemotherapy and whose tumor expresses PD-L1 (CPS  $\geq$  1).

**FF. Renal Cell Carcinoma**

Authorization of 6 months may be granted for treatment of renal cell carcinoma, when either of the following criteria is met:

1. Keytruda will be used as first-line treatment in combination with axitinib for advanced, relapsed or stage IV disease.
2. Keytruda will be used as subsequent therapy in combination with axitinib for relapsed or stage IV disease with clear cell histology.

**GG. Thymic Carcinoma**

Authorization of 6 months may be granted as a single agent for treatment of thymic carcinoma as a second-line agent for unresectable, locally advanced, or metastatic disease.

**HH. Mycosis Fungoides/Sezary Syndrome**

Authorization of 6 months may be granted for treatment of Mycosis Fungoides or Sezary syndrome.

**II. Extranodal NK/T-cell lymphoma, nasal type**

Authorization of 6 months may be granted for treatment of extranodal NK/T-cell lymphoma, nasal type, in members with relapsed or refractory disease.

**JJ. Gestational Trophoblastic Neoplasia**

Authorization of 6 months may be granted as a single agent for treatment of gestational trophoblastic neoplasia for multi-agent chemotherapy-resistant disease when either of the following criteria is met:

1. Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum/etoposide-containing regimen.
2. Member has high-risk disease.

**KK. Poorly Differentiated Neuroendocrine Carcinoma/Large or Small Cell Carcinoma**

Authorization of 6 months may be granted for treatment of poorly differentiated neuroendocrine carcinoma/large or small cell carcinoma in members that have progressed following prior treatment and who have no satisfactory alternative treatment options when either of the following criteria are met:

1. Keytruda will be used for microsatellite instability-high or mismatch repair deficient tumors.
2. Keytruda will be used for tumor mutational burden-high tumors ( $\geq 10$  mutations/megabase).

**LL. Cutaneous Squamous Cell Carcinoma**

Authorization of 6 months may be granted as a single agent for treatment of recurrent or metastatic cutaneous squamous cell carcinoma that is not curable by surgery or radiation.

**MM. Soft Tissue Sarcoma**

Authorization of 6 months may be granted as a single agent for treatment of the following types of soft tissue sarcoma: alveolar soft part sarcoma (ASPS), myxofibrosarcoma, undifferentiated pleomorphic sarcoma (UPS), cutaneous angiosarcoma, and undifferentiated sarcoma.

**NN. Occult Primary Cancer**

Authorization of 6 months may be granted as a single agent for treatment of occult primary cancer in members with microsatellite instability-high or mismatch repair deficient tumors.

**OO. Triple-Negative Breast Cancer**

Authorization of 6 months may be granted for treatment of locally recurrent unresectable or metastatic triple-negative breast cancer when all of the following criteria are met:

1. The diagnosis of triple-negative breast cancer is confirmed by the cancer cells testing negative for ALL of the following receptors:
  - i. Human epidermal growth factor receptor 2 (HER-2)
  - ii. Estrogen
  - iii. Progesterone
2. Tumor must express PD-L1 (CPS  $\geq 10$ ).
3. The requested medication will be used in combination with chemotherapy.

**V. CONTINUATION OF THERAPY**

**A. Adjuvant treatment of melanoma**

Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for cutaneous melanoma who have not experienced disease recurrence or an unacceptable toxicity.

**B. NSCLC, HNSCC, cHL, PMBCL, MSI-H or dMMR Cancers, Gastric Cancer, Esophageal Cancer, Esophagogastric Junction Cancer, Cervical Cancer, HCC, MCC, RCC, Endometrial carcinoma, cSCC, TNBC, TMB-H Cancer**

Authorization of 6 months may be granted (up to 24 months of continuous use) for continued treatment in members requesting reauthorization for NSCLC, SCLC, HNSCC, cHL, PMBCL, MSI-H or dMMR cancers, gastric cancer, esophageal cancer, esophagogastric junction cancer, cervical cancer, HCC, MCC, RCC, endometrial carcinoma, cSCC, TNBC, and TMB-H cancers who have not experienced disease progression or unacceptable toxicity.

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**C. Urothelial Carcinoma**

Authorization of 6 months may be granted (up to 24 months of continuous use) for continued treatment in members requesting reauthorization for urothelial carcinoma when both of the following criteria are met:

1. Member has not experienced disease progression or unacceptable toxicity.
2. For high-risk BCG-unresponsive non-muscle invasive bladder cancer only: disease is not persistent or recurrent.

**D. All other indications**

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who have not experienced disease progression or an unacceptable toxicity.

**VI. REFERENCES**

1. Keytruda [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; May 2021.
2. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 31, 2021.
3. The NCCN Clinical Practice Guidelines in Oncology® Neuroendocrine and Adrenal Tumors 1.2019. ©2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 7, 2020.