

Clinical Policy: Pembrolizumab (Keytruda)

Reference Number: CP.PHAR.322

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Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Pembrolizumab (Keytruda[®]) is a programmed death receptor-1 (PD-1)-blocking antibody.

FDA Approved Indication(s)

Indication	Adults	Pediatrics
Melanoma	X	
Non-small cell lung cancer	X	
Small cell lung cancer	X	
Head and neck squamous cell carcinoma	X	
Classical Hodgkin lymphoma	X	X
Primary mediastinal large B-cell lymphoma	X	X
Urothelial carcinoma	X	
Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancer <i>(First-line treatment for colorectal cancer limited to adults.)</i>	X	X <i>(excludes CNS tumor)</i>
Gastric cancer	X	
Esophageal cancer	X	
Cervical cancer	X	
Hepatocellular carcinoma	X	
Merkel cell carcinoma	X	X
Renal cell carcinoma	X	
Endometrial carcinoma	X	
Tumor mutational burden-high (TMB-H) cancer	X	X <i>(excludes CNS tumor)</i>
Cutaneous squamous cell carcinoma	X	
Adult indications - additional dosing regimens	X	
<i>Off-label uses</i>		
Mycosis fungoides	X	
Sezary syndrome	X	
Anal carcinoma	X	
Gestational trophoblastic neoplasia	X	
Pleural mesothelioma	X	
Extranodal NK/T-cell lymphoma, nasal type	X	
Vulvar carcinoma	X	

**If a solid tumor is characterized as MSI-H, dMMR, or TMB-H, see criteria at Sections I.H or I.P respectively.*

Keytruda is indicated:

- **Melanoma**

- For the treatment of patients with unresectable or metastatic melanoma.
- For the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection.
- **Non-small cell lung cancer (NSCLC)**
 - 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.
 - In combination with carboplatin and either paclitaxel or nab-paclitaxel, as first-line treatment of patients with metastatic squamous NSCLC.
 - As a single agent 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:
 - Stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
 - Metastatic.
 - As a single agent 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.
- **Small cell lung cancer (SCLC)**
 - For the treatment of patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.*
- **Head and neck squamous cell cancer (HNSCC)**
 - In combination with platinum and fluorouracil (FU) for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC.
 - 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) \geq 1] as determined by an FDA-approved test.
 - As a single agent for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum containing chemotherapy.
- **Classical Hodgkin lymphoma (cHL)**
 - For the treatment of adult and pediatric patients with refractory cHL, or who have relapsed after 3 or more prior lines of therapy.*
- **Primary mediastinal large B-cell lymphoma (PMBCL)**
 - For the treatment of adult and pediatric patients with refractory 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.
- **Urothelial carcinoma**
 - 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.*
 - 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.
- 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.
 - **Microsatellite instability-high cancer or mismatch repair deficient cancer**
 - 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, or
 - 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.
 - **Microsatellite instability-high or mismatch repair deficient colorectal cancer (CRC)**
 - For the first-line treatment of patients with unresectable or metastatic MSI-H or dMMR CRC.
 - **Gastric cancer**
 - For the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction (esophagogastric junction; EGJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥ 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, human epidermal growth factor receptor 2 (HER2)/neu-targeted therapy.*
 - **Esophageal cancer**
 - For the treatment of patients with recurrent locally advanced or metastatic squamous cell carcinoma of the esophagus whose tumors express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test, with disease progression after one or more prior lines of systemic therapy.
 - **Cervical cancer**
 - 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.*
 - **Hepatocellular carcinoma (HCC)**
 - For the treatment of patients with HCC who have been previously treated with sorafenib*
 - **Merkel cell carcinoma (MCC)**
 - For the treatment of adult and pediatric patients with recurrent locally advanced or metastatic MCC.*
 - **Renal cell carcinoma (RCC)**
 - For use in combination with axitinib for the first-line treatment of patients with advanced RCC.
 - **Endometrial carcinoma**
 - 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 and are not candidates for curative surgery or radiation.*

- **Tumor mutational burden-high (TMB-H) cancer**
 - 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.
 - Limitations of use: The safety and effectiveness of Keytruda in pediatric patients with TMB-H central nervous system cancers have not been established.
- **Cutaneous squamous cell carcinoma (cSCC)**
 - For the treatment of patients with recurrent or metastatic cSCC that is not curable by surgery or radiation.
- **Adult indications**
 - For use at an additional recommended dosage of 400 mg every 6 weeks for all approved adult indications.**

** 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.*

*** This indication is approved under accelerated approval based on pharmacokinetic data, the relationship of exposure to efficacy, and the relationship of exposure to safety. Continued approval for this dosing may be contingent upon verification and description of clinical benefit in the confirmatory trials.*

Contents:

- I. [Initial Approval Criteria](#)
 - A. [Melanoma](#)
 - B. [Non-Small Cell Lung Cancer](#)
 - C. [Small Cell Lung Cancer](#)
 - D. [Head And Neck Squamous Cell Cancer](#)
 - E. [Classical Hodgkin Lymphoma](#)
 - F. [Primary Mediastinal Large B-Cell Lymphoma](#)
 - G. [Urothelial Carcinoma](#)
 - H. [Microsatellite Instability-High Cancer](#)
 - I. [Gastric, EGJ, and Esophageal Adenocarcinoma](#)
 - J. [Esophageal Squamous Cell Carcinoma](#)
 - K. [Cervical Cancer](#)
 - L. [Hepatocellular Carcinoma](#)
 - M. [Merkel Cell Carcinoma](#)
 - N. [Renal Cell Carcinoma](#)
 - O. [Endometrial Carcinoma](#)
 - P. [Tumor Mutational Burden-High Cancer](#)
 - Q. [Cutaneous Squamous Cell Carcinoma](#)
 - R. [NCCN Recommended Uses \(off-label\)](#)
- II. [Continued Therapy](#)
- III. [Diagnoses/Indications for which coverage is NOT authorized](#)
- IV. [Appendices/General Information](#)
- V. [Dosage and Administration](#)
- VI. [Product Availability](#)
- VII. [References](#)

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Keytruda is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Melanoma (must meet all):

1. Diagnosis of melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Disease is lymph node positive, recurrent, unresectable, or metastatic;
5. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks (for a maximum of 12 months if adjuvant treatment);
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member's renewal date, whichever is longer

B. Non-Small Cell Lung Cancer (must meet all):

1. Diagnosis of NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Disease is recurrent, advanced, or metastatic;
5. If disease is positive for an EGFR, ALK, or ROS1 mutation, disease has progressed on or after targeted therapy (*see Appendix B for examples of targeted therapy*);
6. Keytruda is prescribed in one of the following ways (a or b):
 - a. For PD-L1 positive disease (TPS \geq 1%);
 - b. In combination with a chemotherapy regimen (*see Appendix B*);
7. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member's renewal date, whichever is longer

C. Small Cell Lung Cancer (must meet all):

1. Diagnosis of SCLC;
2. Prescribed by or in consultation with an oncologist;

3. Age \geq 18 years;
4. Disease is unresectable or metastatic;
5. Keytruda is prescribed in one of the following ways (a or b):
 - a. For relapsed disease if no progression on PD-L1 checkpoint inhibitor therapy (e.g., Tecentriq[®] (atezolizumab), Imfinzi[®] (durvalumab));
 - b. For disease that has progressed on or after platinum-based chemotherapy (e.g., cisplatin, carboplatin);
6. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

D. Head and Neck Squamous Cell Carcinoma (must meet all):

1. Diagnosis of HNSCC (*locations include paranasal sinuses, larynx, pharynx, lip, oral cavity, salivary glands; may be occult primary - i.e., primary source unknown*);
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Disease is unresectable, recurrent, or metastatic;
5. Keytruda is prescribed in one of the following ways (a, b, or c):
 - a. In combination with platinum-containing chemotherapy and FU;
 - b. As a first-line single agent and the tumor expresses PD-L1 with a CPS of \geq 1;
 - c. As a single agent for disease that has progressed on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin);
6. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

E. Classical Hodgkin Lymphoma (must meet all):

1. Diagnosis of cHL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age \geq 2 years;
4. Keytruda is prescribed as single-agent therapy in one of the following ways (a or b):
 - a. For disease that is refractory to \geq 1 line of systemic therapy or has relapsed after \geq 3 lines of systemic therapy (*see Appendix B*);
 - b. After hematopoietic stem cell transplant;
5. Request meets one of the following (a, b, or c):*

- a. Adults: Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
- b. Pediatrics: Dose does not exceed 2 mg/kg up to 200 mg every 3 weeks for a maximum of 24 months;
- c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

F. Primary Mediastinal Large B-Cell Lymphoma (must meet all):

1. Diagnosis of PMBCL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age \geq 2 years;
4. Disease is refractory to or has relapsed after \geq 1 line of systemic therapy (*see Appendix B*);
5. Request meets one of the following (a, b, or c):*
 - a. Adults: Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Pediatrics: Dose does not exceed 2 mg/kg up to 200 mg every 3 weeks for a maximum of 24 months;
 - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

G. Urothelial Carcinoma (must meet all):

1. Diagnosis of urothelial carcinoma;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age \geq 18 years;
4. Keytruda is prescribed in one of the following ways (a or b):
 - a. For locally advanced or metastatic disease and member is ineligible for or has previously received platinum-containing chemotherapy (e.g., cisplatin, carboplatin);
 - b. For BCG-unresponsive, high-risk, NMIBC with CIS and member is ineligible for or has elected not to undergo cystectomy (*see Appendix D for BCG shortage information*);
5. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

H. Microsatellite Instability-High/Mismatch Repair Deficient Cancer (must meet all):

1. Diagnosis of a solid tumor classified as MSI-H or dMMR (indicative of MMR gene mutation or loss of expression) (*see Appendix E for examples of MSI-H solid tumors*);
2. Prescribed by or in consultation with an oncologist;
3. Member meets one of the following (a or b):
 - a. Age \geq 2 years to $<$ 18 years and request is not for first-line therapy;
 - b. Age \geq 18 years;
4. Keytruda is prescribed in one of the following ways (a, b, or c):
 - a. As first-line or subsequent therapy for CRC, gallbladder cancer, intrahepatic/extrahepatic cholangiocarcinoma, occult primary tumor;
 - b. As first-line therapy for small bowel adenocarcinoma if oxaliplatin contraindication, otherwise subsequent therapy;
 - c. As subsequent therapy for other solid tumors;
5. Request meets one of the following (a, b, or c):*
 - a. Adults: Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Pediatrics: Dose does not exceed 2 mg/kg up to 200 mg every 3 weeks for a maximum of 24 months;
 - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

I. Gastric, EGJ, and Esophageal Adenocarcinoma (must meet all):

1. Diagnosis of gastric, EGJ, or esophageal adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Disease is unresectable, locally advanced, recurrent, or metastatic;
5. Tumor expresses PD-L1 (CPS \geq 1);
6. Disease has progressed on or after \geq 2 lines of systemic therapy (*see Appendix B*);
7. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

J. Esophageal Squamous Cell Carcinoma (must meet all):

1. Diagnosis of esophageal squamous cell carcinoma;

2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Disease is locally advanced, recurrent, or metastatic;
5. Tumor expresses PD-L1 (CPS \geq 10);
6. Disease has progressed on or after \geq 1 line of systemic therapy (*see Appendix B*);
7. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

K. Cervical Cancer (must meet all):

1. Diagnosis of cervical cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Disease is recurrent or metastatic;
5. Tumor expresses PD-L1 (CPS \geq 1);
6. Disease has progressed on or after \geq 1 line of systemic therapy (*see Appendix B*);
7. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

L. Hepatocellular Carcinoma (must meet all):

1. Diagnosis of HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Disease is classified as Child-Pugh Class A and has progressed on or after therapy with Nexavar[®];
**Prior authorization may be required for Nexavar*
5. Member has not previously been treated with immune checkpoint inhibitor therapy (PD-L1/PD-1, e.g., Tecentriq (atezolizumab), Opdivo (nivolumab));
6. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

M. Merkel Cell Carcinoma (must meet all):

1. Diagnosis of MCC;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 2 years;
4. Disease is recurrent, locally advanced, or metastatic;
5. Request meets one of the following (a, b, or c):*
 - a. Adults: Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Pediatrics: Dose does not exceed 2 mg/kg up to 200 mg every 3 weeks for a maximum of 24 months;
 - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

N. Renal Cell Carcinoma (must meet all):

1. Diagnosis of advanced RCC;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Prescribed in combination with Inlyta[®];
**Prior authorization may be required for Inlyta.*
5. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

O. Endometrial Carcinoma (must meet all):

1. Diagnosis of endometrial carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Prescribed in combination with Lenvima[®]* and disease is not MSI-H or dMMR**
(i.e., disease is not indicative of MMR gene mutation or loss of expression);
**Prior authorization may be required for Lenvima*
***See criteria set I.H. for MSI-H/dMMR endometrial carcinoma*
5. Disease has progressed on or after \geq 1 line of systemic therapy (e.g., carboplatin/paclitaxel);

6. Member is not a candidate for curative surgery or radiation;
7. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

P. Tumor Mutational Burden-High Cancer (must meet all):

1. Diagnosis of a solid tumor classified as TMB-H (i.e., ≥ 10 mutations/megabase [mut/Mb]) (*see Appendix E for examples of TMB-H solid tumors*);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 2 years;
4. Disease is unresectable or metastatic, and has progressed following prior treatment;
5. Request meets one of the following (a, b, or c):*
 - a. Adults: Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Pediatrics: Dose does not exceed 2 mg/kg up to 200 mg every 3 weeks for a maximum of 24 months;
 - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

Q. Cutaneous Squamous Cell Carcinoma (must meet all):

1. Diagnosis of cSCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member is not a candidate for curative surgery or radiation;
5. Request meets one of the following (a or b):*
 - a. Dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

R. NCCN Recommended Uses (off-label) (must meet all):

1. Diagnosis of one of the following (a or b):
 - a. Keytruda is prescribed as first-line or subsequent therapy:

- i. Stage III mycosis fungoides;
 - ii. Stage IV Sezary syndrome;
 - b. Keytruda is prescribed as subsequent therapy:
 - i. Metastatic anal carcinoma;
 - ii. Gestational trophoblastic neoplasia;
 - iii. Malignant pleural mesothelioma;
 - iv. Extranodal NK/T-cell lymphoma, nasal type;
 - v. Metastatic or unresectable thymic carcinoma;
 - vi. Advanced, recurrent, or metastatic PD-L1-positive (CPS \geq 1) vulvar carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

S. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Keytruda for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):*
 - a. Adults (i or ii):
 - i. Melanoma: New dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks (for a maximum of 12 months if adjuvant treatment);
 - ii. All other FDA-approved indications: New dose does not exceed 200 mg every 3 weeks or 400 mg every 6 weeks for a maximum of 24 months;
 - b. Pediatrics: cHL, PMBCL, MSI-H cancer, MCC, TMB-H cancer: New dose does not exceed 2 mg/kg up to 200 mg every 3 weeks for a maximum of 24 months;
 - c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 12 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
- B. Pediatric patients with MSI-H or TMB-H central nervous cancers.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALK: anaplastic lymphoma kinase

BCG: Bacillus Calmette-Guerin

cHL: classical Hodgkin lymphoma

CIS: carcinoma in situ

CNS: central nervous system

CPS: combined positive score

cSCC: cutaneous squamous cell carcinoma

dMMR: mismatch repair deficient

EGFR: epidermal growth factor receptor

FDA: Food and Drug Administration

HCC: hepatocellular carcinoma

HER2: human epidermal growth factor
receptor 2

HNSCC: head and neck squamous cell
carcinoma

MCC: Merkel cell carcinoma

MSI-H: microsatellite instability-high

mut/Mb: mutations/megabase

NCCN: National Comprehensive Cancer
Network

NMIBC: non-muscle invasive bladder cancer

NSCLC: non-small cell lung cancer

PD-1: programmed death protein 1

PD-L1: programmed death-ligand 1

PMBCL: primary mediastinal large B-cell
lymphoma

RCC: renal cell carcinoma

ROS1: ROS proto-oncogene 1

SCLC: small cell lung cancer

TMB-H: tumor mutational burden-high

TPS: tumor proportion score

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<p>Section I.B: Non-Small Cell Lung Cancer Examples of drugs used in combination with Keytruda:</p> <ul style="list-style-type: none"> • Carboplatin, cisplatin, pemetrexed, paclitaxel <p>Examples of targeted therapies:</p> <ul style="list-style-type: none"> • Sensitizing EGFR mutation: erlotinib, afatinib, gefitinib, osimertinib, dacomitinib • ALK mutation: crizotinib, ceritinib, alectinib, brigatinib • ROS1 mutation: crizotinib, ceritinib 	Varies	Varies
<p>Section I.E: Classical Hodgkin Lymphoma Examples of chemotherapy regimens:</p> <ul style="list-style-type: none"> • ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) • Stanford V (doxorubicin, vinblastine, mechlorethamine, etoposide, vincristine, bleomycin, prednisone) • BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone) • AVD (doxorubicin, vinblastine, dacarbazine) • BV (brentuximab vedotin) 	Varies	Varies
<p>Section I.F: Primary Mediastinal Large B-Cell Lymphoma Examples of drugs used in single- or multi-drug chemotherapy regimens:</p> <ul style="list-style-type: none"> • Bendamustine, brentuximab vedotin, carboplatin, cisplatin, cyclophosphamide, cytarabine, dexamethasone, doxorubicin, etoposide, gemcitabine, ibrutinib, ifosfamide, lenalidomide, mesna, mitoxantrone, methylprednisolone, oxaliplatin, prednisone, procarbazine, rituximab, vincristine, vinorelbine* <p><i>*Various combinations of the listed drugs are components of the following chemotherapy regimens: CEOP, CEPP, DHAP, DHAX, EPOCH-R, ESHAP, GDP, GemOx, ICE, MINE, RCDOP, RCEOP, RCEPP, RCHOP, RGCVP</i></p>	Varies	Varies
<p>Section I.G: Urothelial Carcinoma TICE[®] BCG (attenuated, live culture preparation of the Bacillus of Calmette and Guerin strain of <i>Mycobacterium bovis</i> for <i>intravesical</i> use).</p> <p>References for BCG dosing, dosing in the setting of a BCG shortage, and BCG shortage status are listed below and at Appendix D:</p> <ol style="list-style-type: none"> 1. TICE BCG package insert: https://www.fda.gov/vaccines-blood-biologics/vaccines/tice-bcg 2. American Urological Association: Important message about the BCG shortage: https://www.auanet.org/about-us/bcg-shortage-info 3. Centers for Disease Control’s current shortages page: https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-regulated-products-current-shortages 	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<p>Section I.I and I.J: Gastric, EGJ, and Esophageal Cancer Examples of drugs used in single- or multi-drug chemotherapy regimens:*</p> <ul style="list-style-type: none"> • Cisplatin, carboplatin, oxaliplatin, paclitaxel, docetaxel, fluorouracil, capecitabine, irinotecan, leucovorin, epirubicin, ramucirumab (for EGJ adenocarcinoma or esophageal adenocarcinoma only) <p><i>*Trastuzumab may be added to some chemotherapy regimens for HER2 overexpression.</i></p>	Varies	Varies
<p>Section I.K: Cervical Cancer Examples of drugs used in single- or multi-drug chemotherapy regimens:</p> <ul style="list-style-type: none"> • Cisplatin, carboplatin, paclitaxel, docetaxel, bevacizumab, topotecan, fluorouracil, gemcitabine, ifosfamide, irinotecan, topotecan, mitomycin, pemetrexed, vinorelbine 	Varies	Varies
<p>Section I.L: Hepatocellular Carcinoma Nexavar (sorafenib)</p>	400 mg PO BID	800 mg/day
<p>Section I.O: Endometrial Carcinoma Examples of chemotherapy regimens:*</p> <ul style="list-style-type: none"> • Carboplatin/paclitaxel, cisplatin/docetaxel, cisplatin/doxorubicin, carboplatin/paclitaxel/bevacizumab, carboplatin/paclitaxel/trastuzumab, ifosfamide/paclitaxel, cisplatin/ifosfamide, everolimus/letrozole, temsirolimus, Keytruda (pembrolizumab) <p><i>*Individual drugs used in combination regimens may also be used as monotherapy (refer to NCCN Uterine Neoplasms Guidelines)</i></p>	Varies	Varies

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: Keytruda Therapy for Urinary Bladder CIS in the Event of a BCG Shortage

- National Comprehensive Cancer Network (NCCN) information and recommendations:
 - Standard urinary bladder CIS therapy includes lesion resection followed by intravesical BCG.
 - The NCCN advises that in the event of a BCG shortage, BCG should be prioritized for induction of high-risk patients (e.g., high-grade T1 and CIS) and that, if feasible, the dose of BCG may be split (1/3 or 1/2 dose) so that multiple patients may be treated with a single vial in the event of a shortage.
 - If BCG is unavailable, the NCCN recommends the following alternatives:

- Intravesical chemotherapy agents as first-line and subsequent therapy (e.g., gemcitabine, mitomycin, epirubicin, valrubicin, docetaxel, sequential gemcitabine/docetaxel, gemcitabine/mitomycin);
- Initial radical cystectomy if patient is a surgical candidate.
- The NCCN recommendations do not include off-label use of Keytruda as first-line or subsequent therapy in the absence of BCG failure.
- In its BCG June 2020 supply update sent to providers, Merck confirms a path forward to expand BCG manufacturing but cautions that the expansion could take years to fully realize. Merck directs providers to their wholesalers and distributors for supply questions and also provides its National Service Center number (800-672-6372) for additional information.

1. *National Comprehensive Cancer Network Guidelines. Bladder Cancer Version 5.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed July 10, 2020.*
2. *Merck Supply Update: TICE BCG BCG LIVE (for intravesical use). June 2020.*

Appendix E: Examples of Solid Tumors per Pivotal Trials by “N” (descending)

MSI-H Solid Tumors	TMB-H Solid Tumors
CRC	SCLC
Endometrial cancer	Cervical cancer
Biliary cancer	Endometrial cancer
Gastric or GE junction cancer	Anal cancer
Pancreatic cancer	Vulvar cancer
Small intestinal cancer	Neuroendocrine cancer
Breast cancer	Salivary cancer
Prostate cancer	Thyroid cancer
Bladder cancer	Mesothelioma cancer
Esophageal cancer	<i>Additional examples - NCCN compendium: Not currently available.</i>
Sarcoma	
Thyroid cancer	
Retroperitoneal adenocarcinoma	
Small cell lung cancer	
Renal cell cancer	
<i>Additional examples - NCCN compendium: adrenal gland tumor, cervical / vulvar / ovarian / fallopian tube / primary peritoneal cancer, penile cancer, testicular cancer.</i>	

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Melanoma	Adults: 200 mg IV every 3 weeks OR 400 mg every 6 weeks If adjuvant therapy up to 12 months	200 mg every 3 weeks OR 400 mg every 6 weeks
NSCLC, SCLC, HNSCC, cHL, PMBCL, urothelial carcinoma, MSI-H cancer, gastric cancer,	Adults: 200 mg IV every 3 weeks OR 400 mg every 6 weeks up to 24 months	200 mg every 3 weeks OR 400 mg every 6 weeks

Indication	Dosing Regimen	Maximum Dose
esophageal squamous cell carcinoma, cervical cancer, HCC, MCC, cSCC		
cHL, PMBCL, MSI-H cancer, MCC, TMB-H cancer	Pediatrics: 2 mg/kg IV every 3 weeks up to 24 months	200 mg every 3 weeks
RCC	Adults: 200 mg IV every 3 weeks OR 400 mg every 6 weeks in combination with axitinib up to 24 months	200 mg every 3 weeks OR 400 mg every 6 weeks
Endometrial carcinoma	Adults: 200 mg IV every 3 weeks OR 400 mg every 6 weeks in combination with lenvatinib up to 24 months	200 mg every 3 weeks OR 400 mg every 6 weeks

VI. Product Availability

Solution, single-dose vial: 100 mg/4 mL

VII. References

1. Keytruda Prescribing Information. Whitehouse Station, NJ: Merck and Co.; June 2020. Available at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf. Accessed July 10, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at https://www.nccn.org/professionals/drug_compendium/content/. Accessed July 10, 2020.
3. National Comprehensive Cancer Network Guidelines. Cutaneous Melanoma Version 2.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed April 29, 2020.
4. National Comprehensive Cancer Network Guidelines. Uveal Melanoma Version 1.2019. Available at https://www.nccn.org/professionals/physician_gls/pdf/uveal.pdf. Accessed April 29, 2020.
5. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 3.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed April 29, 2020.
6. National Comprehensive Cancer Network Guidelines. Small Cell Lung Cancer Version 3.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Accessed April 29, 2020.
7. National Comprehensive Cancer Network Guidelines. Head and Neck Cancers Version 1.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed April 29, 2020.
8. National Comprehensive Cancer Network Guidelines. Hodgkin Lymphoma Version 2.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed April 29, 2020.
9. National Comprehensive Cancer Network. B-Cell Lymphomas Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed April 29, 2020.

10. National Comprehensive Cancer Network Guidelines. Bladder Cancer Version 5.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed July 10, 2020.
11. National Comprehensive Cancer Network Guidelines. Gastric Cancer Version 1.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed April 29, 2020.
12. National Comprehensive Cancer Network. Esophageal and Esophagogastric Junction Cancers Version 1.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed April 29, 2020.
13. National Comprehensive Cancer Network. Cervical Cancer Version 1.2020. Available at www.nccn.org. Accessed April 29, 2020.
14. National Comprehensive Cancer Network. Hepatobiliary Cancers Version 2.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed April 29, 2020.
15. National Comprehensive Cancer Network Guidelines. Merkel Cell Carcinoma Version 1.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/mcc.pdf. Accessed April 29, 2020.
16. National Comprehensive Cancer Network. Kidney Cancer Version 2.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed April 29, 2020.
17. National Comprehensive Cancer Network. Uterine Neoplasms Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed April 29, 2020.
18. National Comprehensive Cancer Network. Squamous Cell Skin Cancer Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf. Accessed July 6, 2020.
19. Salem ME, Puccini A, Grothey A, et al. Landscape of tumor mutation load, mismatch repair deficiency, and PD-L1 expression in a large patient cohort of gastrointestinal cancers. *Molecular cancer research : MCR*. 2018;16(5):805-812. <https://pubmed.ncbi.nlm.nih.gov/29523759/>

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9271	Injection, pembrolizumab, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.182 Excellus Oncology. Non-small cell lung cancer: NCCN off-label recommendations added; “recurrent or” added to “metastatic disease” and “or unknown” added	01.17	03.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
to “negative mutation status” to consolidate criteria of those FDA/NCCN uses that differed by the referenced terms. Head and neck cancers: NCCN off-label recommended uses added; subtypes by location outlined at Appendix B.		
Created criteria for new FDA indications: cHL, urothelial carcinoma, and MSI-H cancer. Melanoma: modified max dose from 2 mg/kg to 200 mg per package insert. NSCLC: added criteria for updated FDA indication (non-squamous metastatic disease). HNSCC: specified that recommended NCCN off-label uses pertain to non-nasopharyngeal cancer. All indications: added max dose requirement to both initial and re-auth criteria. Increased all approval durations from 3/6 months to 6/12 months. Removed reasons to discontinue. Added requirement for documentation of positive response to therapy.	05.17	08.17
Created criteria for new FDA indications per PI and NCCN: Gastric Cancer	10.17	11.17
Criteria added for new FDA indications cervical cancer and primary mediastinal large B-cell lymphoma; urothelial carcinoma criteria updated for use in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status; added Commercial line of business; added age and specialist prescribing for all indications; applied oncology streamlining approach; added HIM-Medical Benefit line of business; reference reviewed and updated.	07.17.18	08.18
4Q 2018 annual review: no significant changes; references reviewed and updated.	07.26.18	11.18
Added requirement for negative or unknown EGFR, ALK, ROS1, or BRAF tumor status per updated FDA indication and NCCN compendium for first-line use in metastatic nonsquamous NSCLC in combo with platinum chemotherapy and pemetrexed; streamlined criteria for subsequent use in NSCLC; references reviewed and updated.	10.02.18	02.19
Criteria added for new FDA indications HCC and as first-line therapy for metastatic squamous NSCLC in combination with chemotherapy; re-added criteria for PMBCL as previously approved; references reviewed and updated.	11.27.18	02.19
No clinical changes: off-label designation removed for MCC as it is now FDA approved.	01.31.19	02.19
Criteria added for new FDA indications: 1) melanoma for adjuvant treatment is incorporated by adding lymph node positive disease; complete resection is not required given additional NCCN recommended uses; age is adjusted from 2 to 18 years and older per	04.23.19	05.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>the FDA label’s indication and pediatric sections; 2) renal cell carcinoma; 3) advanced (stage III) NSCLC.</p> <p>NSCLC: single-agent therapy for brain metastasis is added per NCCN; removal of histology requirements; mutational status requirements are limited to EGFR and ALK per the FDA label for primary therapy and to the additional NCCN directed requirement of prior ROS1 targeted therapy; subsequent therapy requirement for platinum-based chemotherapy when TPS \geq 1% is removed since Keytruda is now FDA-approved as first-line therapy when TPS \geq 1%.</p> <p>HNSCC: locations as examples are incorporated into the criteria set; oxaliplatin is removed as an example as it is not listed as an NCCN recommendation for this cancer.</p> <p>cHL and PMBCL: refractory disease is clarified by specifying at least one line of therapy; transplantation is included as a line of therapy option.</p> <p>Urothelial carcinoma: progression as a response to platinum therapy is removed as response may include persistence or partial response.</p> <p>MSI-H cancer: appendix updated to include solid tumors listed in the NCCN compendium and FDA label; subsequent therapy requirement is removed where recommended per NCCN; disease characteristics (e.g., metastatic) are removed to encompass NCCN recommended uses.</p> <p>Gastric cancer: esophageal cancer and unresectable disease are added; systemic therapy examples are expanded per NCCN.</p> <p>Cervical cancer: chemotherapy examples are expanded per NCCN. Additional NCCN recommended uses are added as a new Section L with notation of primary versus subsequent therapy requirements. Appendix B and references reviewed and updated.</p>		
<p>Added pediatric maximum dosing recommendations for all indications applicable to pediatrics: cHL, PMBCL, MSI-H cancer, and MCC.</p>	05.06.19	
<p>Criteria added for new FDA indications: 1) SCLC (previously included per NCCN as subsequent therapy; updated criteria maintains subsequent therapy but specifies prior platinum therapy; 2) HNSCC (previously post platinum therapy only; new indications include first-line combination therapy and first-line single-agent therapy, the latter if PD-L1 \geq 1. Disease characteristics for HNSCC are updated from recurrent or metastatic, to unresectable, recurrent or metastatic; 3) dosing for all indications is limited to 24 months per the PI with the exception of melanoma and off-label uses in section I.N; 4) dosing for adjuvant melanoma therapy is limited to 12 months per the PI; 5) boilerplate language is added to all dosing sections: “Prescribed regimen must be FDA-approved or recommended by NCCN”; references reviewed and updated.</p>	07.09.19	08.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2019 annual review: criteria added for new FDA indication for esophageal squamous cell carcinoma; criteria added for new FDA indication in endometrial carcinoma; added chondrosarcomas as another example of an NCCN-supported MSI-H/dMMR tumor type in <i>Appendix D</i> ; references reviewed and updated.	10.15.19	11.19
Criteria added for new FDA indication: NMIBC-CIS; urologist added for UC; HIM line of business added; removed 50 mg powder single-dose vial formulation; references reviewed and updated.	02.11.20	05.20
3Q 2020 annual review: new FDA approved dosing of 400 mg every 6 weeks added to all labeled adult indications; NSCLC: first-line removed from combination with chemotherapy per NCCN; brain metastasis moved under PD-L1 positive disease per NCCN; SCLC: relapsed disease added per NCCN; cHL: Keytruda as single-agent therapy added per NCCN; HNSCC: first-line therapy requirement removed from combination platinum/FU therapy per NCCN; MSI-H/dMMR tumors: first-line therapy for occult primary tumor and small bowel added per NCCN; HCC: Child-Pugh Class A added per NCCN/pivotal trial with no prior checkpoint inhibitor therapy caveat per NCCN; three new FDA approved indications added: 1) MSI-H/dMMR CRC first-line (adults), 2) TMB-H (adults/pediatrics), 3) cSCC (adults); NCCN off-label Keytruda use as first-line for MSI-H tumors is limited to adults; NCCN off-label criteria set is limited to adults; endometrial carcinoma criteria set is limited to 24 months of therapy; MSI-H/TMB-H CNS tumors excluded for pediatrics per PI; indication table added with directives to MSI-H/TMB-H criteria sets for appropriate cancers; BCG appendix D added; TMB-H solid tumor examples added to appendix E; references reviewed and updated.	07.14.20	08.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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Note:

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