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	X
Non-small cell lung cancer	X	
Malignant pleural mesothelioma (MPM)	X	
Head and neck squamous cell carcinoma (HNSCC)	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 *(First-line treatment for colorectal cancer limited to adults.)*	X	X
Gastric cancer	X	
Esophageal cancer	X	
Cervical cancer	X	
Hepatocellular carcinoma	X	
Biliary tract cancer	X	
Merkel cell carcinoma	X	X
Renal cell carcinoma	X	
Endometrial carcinoma	X	
Tumor mutational burden-high (TMB-H) cancer	X	X *(excludes CNS tumor)*
Cutaneous squamous cell carcinoma	X	
Triple-negative breast cancer (TNBC)	X	
Off-label uses		
Adrenocortical carcinoma	X	
Alveolar soft part sarcoma	X	
Anal carcinoma	X	
Angiosarcoma	X	
Anaplastic carcinoma	X	
Anaplastic large cell lymphoma	X	
Central nervous system cancers	X	
Extranodal NK/T-cell lymphoma	X	
Gestational trophoblastic neoplasia	X	

Indication	Adults	Pediatrics
Kaposi sarcoma	X	
Mycosis fungoides	X	
Ovarian cancer, fallopian tube cancer, primary peritoneal cancer	X	
Penile cancer	X	
Peritoneal mesothelioma	X	
Sezary syndrome	X	
Small cell lung cancer	X	
Soft tissue sarcoma	X	
Thymic carcinoma	X	
Thyroid carcinoma	X	
Vaginal cancer	X	
Vulvar carcinoma	X	
Glioma		X

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

Keytruda is indicated:

- **Melanoma**
  - For the treatment of patients with unresectable or metastatic melanoma.
  - For the adjuvant treatment of adult and pediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma 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 paclitaxel protein-bound, 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) ≥ 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 ≥ 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.
  - For the treatment of patients with resectable (tumors ≥ 4 cm or node positive) NSCLC in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.
  - As a single agent for the adjuvant treatment following resection and platinum-based chemotherapy for adult patients with Stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC.

- **Malignant pleural mesothelioma (MPM)**
  - In combination with pemetrexed and platinum chemotherapy, as first-line treatment of adult patients with unresectable advanced or metastatic MPM.
- **Head and neck squamous cell cancer (HNSCC)**
  - For the treatment of adult patients with resectable locally advanced HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test, as a single agent as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without cisplatin and then as a single agent
  - 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 (CPS ≥ 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 patients with relapsed or refractory cHL.
  - For the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more 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**
  - In combination with enfortumab vedotin for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma.
  - As a single agent for the treatment of patients with locally advanced or metastatic urothelial carcinoma:
    - who are not eligible for any platinum-containing chemotherapy, or
    - who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
  - As a single agent 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 (MSI-H) or mismatch repair deficient (dMMR) cancer**
  - For the treatment of adult and pediatric patients with unresectable or metastatic, MSI-H or dMMR solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.
- **Microsatellite instability-high or mismatch repair deficient colorectal cancer (CRC)**
  - For the treatment of patients with unresectable or metastatic MSI-H or dMMR CRC as determined by an FDA-approved test.

- **Gastric cancer**
  - 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 whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
  - In combination with fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
- **Esophageal cancer**
  - For the treatment of patients with locally advanced or metastatic esophageal or GEJ (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either:
    - In combination with platinum- and fluoropyrimidine-based chemotherapy whose tumors express PD-L1 (CPS ≥ 1), or
    - 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.
- **Cervical cancer**
  - In combination with chemoradiotherapy (CRT) for the treatment of patients with locally advanced cervical cancer involving the lower third of the vagina, with or without extension to pelvic sidewall, or hydronephrosis/non-functioning kidney or spread to adjacent pelvic organs (FIGO 2014 Stage III-IVA).
  - 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.
  - 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.
- **Hepatocellular carcinoma (HCC)**
  - For the treatment of patients with HCC secondary to hepatitis B who have received prior systemic therapy other than a PD-1/PD-L1-containing regimen.
- **Biliary tract cancer (BTC)**
  - In combination with gemcitabine and cisplatin for the treatment of patients with locally advanced unresectable or metastatic BTC.
- **Merkel cell carcinoma (MCC)**
  - For the treatment of adult and pediatric patients with recurrent locally advanced or metastatic MCC.
- **Renal cell carcinoma (RCC)**
  - In combination with axitinib, for the first-line treatment of adult patients with advanced RCC.
  - In combination with lenvatinib, for the first-line treatment of adult patients with advanced RCC.
  - 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.

- **Endometrial carcinoma**
  - In combination with carboplatin and paclitaxel, followed by Keytruda as a single agent, for the treatment of adult patients with primary advanced or recurrent endometrial carcinoma.
  - In combination with lenvatinib, for the treatment of patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) or not MSI-H as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.
  - As a single agent for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting 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 or locally advanced cSCC that is not curable by surgery or radiation.
- **Triple-negative breast cancer (TNBC)**
  - For the 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.
  - In combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥ 10) as determined by an FDA approved test.
- **Adult cHL and adult PMBCL**
  - For use at an additional recommended dosage of 400 mg every 6 weeks for cHL and PMBCL in adults.**

** 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:

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 ≥ 12 years;
4. Disease is Stage IIB, IIC, III, recurrent, unresectable, or metastatic;
5. Prescribed as one of the following (a, b, or c):
   a. A single agent;
   b. In combination with Lenvima® or Yervoy®;
   c. In combination with Mekinist® and Trafinlar® for disease with BRAF V600 activating mutation;
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 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 ≥ 18 years;
4. One of the following (a or b):
   a. Disease is resectable or resected;
   b. Disease is recurrent, advanced, or metastatic, and request meets one of the following (i, ii, iii, iv, v, or vi):
      i. Disease mutation status is positive for EGFR exon 20, KRAS G12C, NRTK1/2/3, BRAF V600E, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2);
      ii. Disease mutation status is positive for EGFR S768I, L861Q, and/or G719X, and member has received prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib;*
      iii. Disease mutation status is positive for EGFR exon 19 deletion or L858R, and member has received prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, dacomitinib, or amivantamab-vmjw + lazertinib;*
      iv. Disease mutation status is positive for ROS1 rearrangement, and member has received prior crizotinib, entrectinib, or repotrecitinib;*
      v. Disease mutation status is positive for ALK rearrangement, and member has received prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib;*
   **Prior authorization may be required*
5. Keytruda is prescribed in one of the following ways (a, b, c, d, or e):
   a. For PD-L1 positive disease (TPS ≥ 1%);
   b. In combination with a chemotherapy regimen *(see Appendix B)*;
   c. In combination with a chemotherapy regimen *(see Appendix B)* as neoadjuvant treatment, followed by single-agent adjuvant treatment after surgery for patients with resectable (tumors ≥ 4 cm or node positive) disease;
   d. As single-agent continuation maintenance therapy if previously given first line as part of a chemotherapy regimen;
   e. As single-agent adjuvant treatment following resection and platinum-based chemotherapy (e.g., cisplatin, carboplatin) for adult patients with stage IB (T2a ≥ 4 cm), II, or IIIA disease;
6. Member does not have contraindications to PD-1/PD-L1 inhibitor therapy (e.g., Opdivo®, Yervoy, Tecentriq®, Imfinzi®) (*see Appendix F*);
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 duration of one of the following (i, ii, or iii):
      i. Adjuvant therapy: 12 months;
      ii. Neoadjvuant, followed by adjuvant treatment: 12 weeks (neoadjuvant), then 39 weeks (adjuvant treatment);

iii. All other requests: 24 months;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

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Approval duration:
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C. Malignant Pleural Mesothelioma (must meet all)**:**

1. Diagnosis of MPM;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is unresectable, advanced, or metastatic;
5. Keytruda is prescribed in combination with pemetrexed and platinum-containing chemotherapy;
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:
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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 ≥ 18 years;
4. Disease is resectable, locally advanced, unresectable, recurrent/persistent, or metastatic;
5. For unresectable, recurrent/persistent, or metastatic disease, Keytruda is prescribed in one of the following ways (a, b, c, or d):
   a. In combination with platinum-containing chemotherapy and either FU, docetaxel, or gemcitabine;
   b. In combination with Erbitux® as first-line therapy or subsequent-line therapy (*off-label)*;
   c. As a first-line single agent and the tumor expresses PD-L1 with a CPS of ≥ 1;
   d. As a single agent for disease that has progressed on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin);

6. For resectable locally advanced disease, all of the following (a, b, and c):
   a. Tumor expresses PD-L1 with a CPS of ≥ 1;
   b. Prescribed initially for neoadjuvant therapy as a single agent;
   c. Then continued as adjuvant therapy in combination with RT with or without cisplatin, then as a single agent;
7. For nasopharyngeal carcinoma, one of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395.*
   a. Failure of Loqtorzi® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Request is for treatment associated with cancer for a state with regulations against step therapy in certain oncology settings (*see Appendix G*);
8. 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 one of the following (i, ii, or iii):
      i. Neoadjuvant therapy: 6 weeks;
      ii. Adjuvant therapy: 1 year;
      iii. All other requests: 24 months;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

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E. Classical Hodgkin Lymphoma (must meet all)**:**
1. Diagnosis of cHL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 6 months;
4. Keytruda is prescribed as single-agent therapy (*adults or pediatrics*) or in combination with GVD (gemcitabine, vinorelbine, liposomal doxorubicin), ICE (ifosfamide, carboplatin, etoposide), decitabine and vorinostat (*adults only*) in one of the following ways (a, b, c, or d):
   a. For palliative therapy;
   b. Post-allogeneic hematopoietic cell transplant or post-autologous stem cell rescue;
   c. Member is not a candidate for anthracycline;
   d. For disease that is relapsed or refractory to ≥ 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)*.

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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 ≥ 6 months;
4. Disease is refractory to or has relapsed after ≥ 1 line of systemic therapy *(see Appendix B)*;
5. Prescribed in one of the following ways (a or b):
   a. As a single agent;
   b. For age ≥ 6 months to < 18 years only, in combination with Adcetris®;
6. 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)*.

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G. Urothelial Carcinoma (must meet all)**:**
1. Diagnosis of urothelial carcinoma;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. Keytruda is prescribed in one of the following ways (a, b, c, or d):
   a. In combination with Padcev®, Inlyta®, or Lenvima® for locally advanced, relapsed, or metastatic disease;*
      **Prior authorization may be required for Padcev, Inlyta and Lenvima.*
   b. As a single agent for locally advanced or metastatic disease, and member is ineligible for or has previously received platinum-containing chemotherapy (e.g., cisplatin, carboplatin) or previously received other chemotherapy;
   c. As a single agent for the treatment of 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*);
   d. As a single agent for adjuvant therapy;
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*).

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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 ≥ 6 months to < 18 years and request is not for first-line therapy;
   b. Age ≥ 18 years;
4. Keytruda is prescribed in one of the following ways (a or b):
   a. As first-line or subsequent therapy for ampullary adenocarcinoma, CRC, gallbladder cancer, gastric cancer, GEJ cancer, intrahepatic/extrahepatic cholangiocarcinoma, non-nasopharyngeal head, and neck cancer, occult primary tumor, pancreatic adenocarcinoma, or small bowel adenocarcinoma;
   b. As subsequent therapy for other solid tumors;
5. Prescribed in one of the following ways (a or b):
   a. As a single agent;
   b. For gastric or GEJ cancers: as a single agent or in combination with platinum- and fluoropyrimidine-based chemotherapy;
6. 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*).

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I. Gastric Cancer, Esophageal Cancer, or Gastroesophageal Junction Cancer (must meet all)**:**
1. Diagnosis of gastric cancer, esophageal cancer, or GEJ cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. Disease is unresectable, locally advanced, recurrent, or metastatic;
   b. Member is planned for esophagectomy;
5. Member meets one of the following (a, b, or c):
   a. Keytruda is prescribed in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, and both (i and ii):
      i. HER2-positive gastric or GEJ adenocarcinoma;
      ii. Tumor expresses PD-L1 (CPS ≥ 1);

b. Both of the following (i and ii):
   i. Keytruda is prescribed in combination with platinum- and fluoropyrimidine-based chemotherapy, and both (1 and 2):
      1) One of the following (a or b):
         a. HER2-negative gastric or GEJ adenocarcinoma;
         b. Esophageal carcinoma or GEJ squamous cell carcinoma;
      2) Tumor expresses PD-L1 (CPS ≥ 1);
   ii. One of the following (1 or 2):
      1) Failure of Tevimbra® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      2) Request is for treatment associated with cancer for a state with regulations against step therapy in certain oncology settings (*see Appendix G*);

c. Keytruda is prescribed as a single agent after one or more prior lines of systemic therapy for members with tumors of squamous cell GEJ that express PD-L1 (CPS ≥ 10) *(see Appendix B)*;

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)*.

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J. Cervical Cancer (must meet all)**:**
1. Diagnosis of cervical cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in one of the following ways (a, b, c, or d):
   a. As a single agent, and all of the following (i, ii, and iii):
      i. Tumor expresses PD-L1 (CPS ≥ 1);
      ii. Disease is recurrent or metastatic;
      iii. Disease has progressed on or after ≥ 1 line of systemic therapy *(see Appendix B)*;
   b. In combination with chemotherapy (e.g., paclitaxel/cisplatin, paclitaxel/carboplatin) with or without bevacizumab, and both (i and ii):
      i. Tumor expresses PD-L1 (CPS ≥ 1);
      ii. Disease is persistent, recurrent, or metastatic;
   c. In combination with Tivdak®, and all of the following (i, ii, and iii):
      i. Tumor expresses PD-L1 (CPS ≥ 1) and has not received prior immune-oncology therapy;
      ii. Disease is recurrent or metastatic;
      iii. Disease has progressed on or after ≥ 1 line of systemic therapy *(see Appendix B)*;

d. In combination with CRT, and (i):
   i. Disease is FIGO 2014 Stage III-IVA or FIGO 2018 stage III-IVA (*see Appendix F*);

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*).

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

K. Hepatocellular Carcinoma (must meet all):
1. Diagnosis of HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. Prescribed as subsequent-line systemic therapy and (i):
      i. Member has not previously been treated with immune checkpoint inhibitor therapy (PD-L1/PD-1, e.g., Tecentriq, Opdivo);

      **Prior authorization may be required for Nexavar, Lenvima and Stivarga*
   b. Prescribed as first line treatment;
5. Prescribed as a single agent;
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)*.

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L. Biliary Tract Cancer (must meet all):
1. Diagnosis of BTC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. Disease is locally advanced unresectable or resected gross residual (R2) disease, or metastatic;
   b. Disease is resectable locoregionally advanced and prescribed as neoadjuvant therapy for gallbladder cancer;
5. Prescribed in combination with gemcitabine and cisplatin;
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 ≥ 6 months;
4. Disease is recurrent, locally advanced, or metastatic;
5. Prescribed as a single agent;
6. 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 RCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Keytruda is prescribed in one of the following ways (a, b, or c):
   a. In combination with Inlyta or Lenvima*, and disease is advanced (i.e., relapsed or stage IV);
      **Prior authorization may be required for Inlyta and Lenvima.*
   b. As single-agent adjuvant treatment, and member is at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions;
   c. As a single agent for relapsed or stage IV disease with non-clear cell histology (off-label);
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 (combination therapy) or 12 months (monotherapy);
   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 ≥ 18 years;
4. Prescribed in one of the following (a or b):
   a. In combination with Lenvima* and both of the following (i and ii):
      **Prior authorization may be required for Lenvima*
      i. Disease is pMMR or not MSI-H;
         **See criteria set I.G. for MSI-H/dMMR endometrial carcinoma*
      ii. Progressed following prior systemic therapy (e.g., carboplatin/paclitaxel);
   b. In combination with carboplatin and paclitaxel and continued as a single agent for maintenance therapy for advanced, recurrent, or Stage III-IV disease;
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

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 ≥ 6 months;
4. Disease is unresectable or metastatic;
5. One of the following (a or b):
   a. Disease has progressed following prior treatment;
   b. Prescribed as a first-line therapy for ampullary adenocarcinoma or pancreatic adenocarcinoma;
6. Prescribed as a single agent;
7. 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. Prescribed as a single agent;
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

R. Triple Negative Breast Cancer (must meet all)**:**
1. Diagnosis of TNBC (i.e., estrogen receptor/progesterone receptor [ER/PR] negative and human epidermal growth factor receptor 2 [HER2]-negative);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. One of the following (a, b, or c):
   a. Disease is high-risk early-stage (*see Appendix F*), and (i):
      i. Prescribed in combination with chemotherapy (e.g., carboplatin, paclitaxel, doxorubicin, cyclophosphamide) as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery;
   b. Disease is locally recurrent unresectable or metastatic, and both of the following (i and ii):
      i. Tumor expresses PD-L1 (CPS ≥ 10);
      ii. Prescribed in combination with chemotherapy (e.g., paclitaxel, paclitaxel protein-bound, gemcitabine and carboplatin);
   c. Prescribed as preoperative systemic therapy in combination with carboplatin and docetaxel;
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 (i or ii):
      i. High-risk, early-stage TNBC: 24 weeks as neoadjuvant therapy and 27 weeks as adjuvant therapy;
      ii. Locally recurrent unresectable or metastatic TNBC: 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

S. Pediatric Glioma (off-label) (must meet all):
1. Diagnosis of hypermutant tumor diffuse high-grade glioma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 6 months and < 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

T. NCCN Recommended Uses (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. Keytruda is prescribed as first-line or subsequent therapy:
      i. Central nervous system (CNS) cancer (e.g., brain metastases);
      ii. Stage IA - III mycosis fungoides;
      iii. Stage IV Sezary syndrome;
      iv. Unresectable or metastatic adrenocortical carcinoma;
      v. Alveolar soft part sarcoma;
      vi. Angiosarcoma;
      vii. Thymic carcinoma, and prescribed as a single agent;
      viii. Thyroid carcinoma;
      ix. Metastatic anaplastic carcinoma;
      x. Vaginal cancer;
      xi. Peritoneal mesothelioma, and prescribed in combination with platinum-containing chemotherapy and pemetrexed;
      xii. Recurrent or metastatic penile cancer, and prescribed in combination with fluorouracil and platinum-containing chemotherapy;
   b. Keytruda is prescribed as single-agent subsequent therapy:
      i. Metastatic anal carcinoma, and member has not previously received Keytruda or Opdivo;
      ii. Gestational trophoblastic neoplasia;
      iii. Extranodal NK/T-cell lymphoma;
      iv. Advanced, recurrent, or metastatic PD-L1-positive (CPS ≥ 1) vulvar carcinoma;
      v. Relapsed or refractory cutaneous anaplastic large cell lymphoma;
      vi. Relapsed or primary progressive small cell lung cancer;
      vii. Kaposi sarcoma;
      viii. Soft tissue sarcoma subtypes: Myxofibrosarcoma, undifferentiated pleomorphic sarcoma (UPS), dedifferentiated liposarcoma, cutaneous angiosarcoma, and undifferentiated sarcomas;
   c. Keytruda is prescribed in combination with cyclophosphamide and bevacizumab for platinum-resistant persistent ovarian cancer, fallopian tube cancer, primary peritoneal cancer;
2. Prescribed by or in consultation with an oncologist;

3. Age ≥ 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

U. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 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. Member has NOT received the maximum duration of therapy as described below (a, b, c, d, or e):
   a. Adjuvant melanoma treatment or RCC monotherapy: up to 12 months;
   b. For high-risk, early stage TNBC: up to 24 weeks if neoadjuvant treatment, followed by 27 weeks as adjuvant treatment;
   c. NSCLC, one of the following (i, ii, or iii):
      i. Adjuvant treatment: 12 months;
      ii. Neoadjuvant, followed by adjuvant treatment: 12 weeks (neoadjuvant), then 39 weeks (adjuvant treatment);
      iii. All other requests: 24 months;
   d. HNSCC, one of the following (i, iii, or iii):
      i. Neoadjuvant treatment: 6 weeks;
      ii. Adjuvant treatment: 1 year;

iii. All other requests: 24 months;
e. All other FDA-approved indications: up to 24 months;

4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. Adults (i or ii):
      i. New dose does not exceed 200 mg every 3 weeks;
      ii. New dose does not exceed 400 mg every 6 weeks;
   b. Pediatrics: New dose does not exceed 2 mg/kg up to 200 mg every 3 weeks;
   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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 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.PA.154 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
BTC: biliary tract cancer
cHL: classical Hodgkin lymphoma
CIS: carcinoma in situ
CNS: central nervous system
CPS: combined positive score
CRC: colorectal cancer
CRT: chemoradiotherapy
cSCC: cutaneous squamous cell carcinoma

dMMR: mismatch repair deficient
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
GEJ: gastroesophageal junction
HCC: hepatocellular carcinoma
HER2: human epidermal growth factor receptor 2
HNSCC: head and neck squamous cell carcinoma
MCC: Merkel cell carcinoma
MPM: malignant pleural mesothelioma
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
pMMR: mismatch repair proficient
RCC: renal cell carcinoma
ROS1: ROS proto-oncogene 1
TMB-H: tumor mutational burden-high
TNBC: triple-negative breast cancer
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
Section I.B: Non-Small Cell Lung Cancer Examples of drugs used in combination with Keytruda: • Carboplatin, cisplatin, pemetrexed, paclitaxel Examples of targeted therapies: • EGFR S768I, L861Q, and/or G719X targeted therapies: afatinib, osimertinib, erlotinib, gefitinib, dacomitinib • EGFR exon 19 deletion or L858R targeted therapies: erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, dacomitinib, or amivantamab-vmjw + lazertinib • ROS1 targeted therapies: crizotinib, entrectinib, repotrecitnib • ALK rearrangement targeted therapies: crizotinib, ceritinib, alectinib, brigatinib, lorlatinib	Varies	Varies
Section I.D: Head and Neck Squamous Cell Carcinoma Nasopharyngeal carcinoma (NPC) • Loqtorzi (toripalimab-tpzi)	<u>First-line treatment for NPC:</u> 240 mg IV every three weeks up to 24 months in combination with	<u>First-line treatment for NPC:</u> 240 mg/3 weeks <u>Previously treated,</u>

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	cisplatin and gemcitabine Previously treated, unresectable or metastatic NPC 3 mg/kg IV every two weeks	unresectable or metastatic NPC 3 mg/kg every two weeks
Section I.E: Classical Hodgkin Lymphoma Adults: Examples of chemotherapy regimens: • ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) • Stanford V (doxorubicin, vinblastine, mechlorethamine, etoposide, vincristine, bleomycin, prednisone) • BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, probarbazine, prednisone) • Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine) Pediatrics: Examples of chemotherapy regimens • AVPC (doxorubicin, vincristine, prednisone, cyclophosphamide) • ABVE-PC (doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide) • Brentuximab vedotin + bendamustine • ICE (ifosfamide, carboplatin, etoposide)	Varies	Varies
Section I.F: Primary Mediastinal Large B-Cell Lymphoma Examples of drugs used in single- or multi-drug chemotherapy regimens: • Bendamustine, brentuximab vedotin, carboplatin, cisplatin, cyclophosphamide, cytarabine, dexamethasone, doxorubicin, etoposide, gemcitabine, ibrutinib, ifosfamide, lenalidomide, mesna, mitoxantrone, methylprednisolone, oxaliplatin, prednisone, procarbazine, rituximab, vincristine, vinorelbine* **Various combinations of the listed drugs are components of the following chemotherapy regimens: CEOP, CEPP, DHAP, DHAX,*	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
EPOCH-R, ESHAP, GDP, GemOx, ICE, MINE, RCDOP, RCEOP, RCEPP, RCHOP, RGCVP		
Section I.G: Urothelial Carcinoma TICE® BCG (attenuated, live culture preparation of the Bacillus of Calmette and Guerin strain of *Mycobacterium bovis* for ***intravesical*** use). References for BCG dosing, dosing in the setting of a BCG shortage, and BCG shortage status are listed below and at Appendix D: 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
Section I.I: Gastric, EGJ, and Esophageal Cancer Examples of drugs used in single- or multi-drug chemotherapy regimens:* • Cisplatin, carboplatin, oxaliplatin, paclitaxel, docetaxel, fluorouracil, capecitabine, irinotecan, leucovorin, epirubicin, ramucirumab (for EGJ adenocarcinoma or esophageal adenocarcinoma only) **Trastuzumab may be added to some chemotherapy regimens for HER2 overexpression.*	Varies	Varies
Section I.I: Gastric, EGJ, and Esophageal Cancer Tevimbra (tislelizumab-jsgr)	200 mg IV on Day 1 of every 3-week cycle	See regimen
Section I.J: Cervical Cancer Examples of drugs used in single- or multi-drug chemotherapy regimens: • Cisplatin, carboplatin, paclitaxel, docetaxel, bevacizumab, topotecan, fluorouracil, gemcitabine, ifosfamide, irinotecan, topotecan, mitomycin, pemetrexed, vinorelbine Examples of CRT regimens: • Cisplatin plus external beam radiation therapy (EBRT), followed by brachytherapy (BT)	Varies	Varies
Section I.K: Hepatocellular Carcinoma Nexavar (sorafenib)	400 mg PO BID	800 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Section I.K: Hepatocellular Carcinoma Lenvima (lenvatinib)	12 mg PO QD (patients ≥ 60 kg) or 8 mg PO QD (patients < 60 kg)	12 mg/day
Section I.K: Hepatocellular Carcinoma Stivarga (regorafenib)	160 mg PO QD for the first 21 days of each 28-day cycle	160 mg/day on days 1 to 21, every 28 days
Section I.K: Hepatocellular Carcinoma Cabometyx (cabozantinib)	60 mg PO QD	60 mg/day
Section I.O: Endometrial Carcinoma Examples of chemotherapy regimens:* • Carboplatin/paclitaxel, cisplatin/docetaxel, cisplatin/doxorubicin, carboplatin/paclitaxel/bevacizumab, carboplatin/paclitaxel/trastuzumab, ifosfamide/paclitaxel, cisplatin/ifosfamide, everolimus/letrozole, temsirolimus, Keytruda (pembrolizumab) **Individual drugs used in combination regimens may also be used as monotherapy (refer to NCCN Uterine Neoplasms Guidelines)*	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 1.2025. Available at* https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed May 29*, 2025.*
2. *Merck Supply Update: TICE 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	Small cell lung cancer
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	*Additional examples – NCCN compendium*: Adrenal tumor, ampullary adenocarcinoma, breast cancer, ovarian / fallopian tube / primary peritoneal cancer, chondroma, chondrosarcoma, head and neck cancer, Ewing sarcoma, nasopharynx cancer, occult primary carcinoma, osteosarcoma, pancreatic cancer, prostate cancer, testicular cancer, small bowel adenocarcinoma, soft tissue sarcoma, uterine sarcoma, vaginal cancer
Sarcoma	
Thyroid cancer	
Retroperitoneal adenocarcinoma	
Small cell lung cancer	
Renal cell cancer	
Additional examples – NCCN compendium: Adrenal tumor, ampullary adenocarcinoma, cervical / vulvar / ovarian / fallopian tube / primary peritoneal cancer, chondrosarcoma, chondroma, Ewing sarcoma, head and neck cancer, hepatocellular carcinoma, neuroendocrine cancer, occult primary carcinoma, osteosarcoma, penile cancer, small bowel adenocarcinoma, soft tissue sarcoma, testicular cancer, vaginal cancer	

Appendix F: General Information

- High-risk early-stage TNBC was defined as tumor size > 1 cm but ≤ 2 cm in diameter with nodal involvement or tumor size > 2 cm in diameter regardless of nodal involvement in the pivotal KEYNOTE-522 study.
- Although Keytruda's approval for small cell lung cancer was withdrawn due to lack improvement in overall survival in phase 3 randomized trial data, the NCCN continues to

recommend this use, stating that "pembrolizumab [is] just as effective as, and sometimes better than, the other subsequent therapy options."

- Per NCCN, contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, or presence of an oncogene (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements), which has been shown to be associated with less benefit.
- FIGO 2014 and 2018 stages:
  - FIGO 2014 Stage III-IVA locally advanced cervical cancer is defined as tumor involvement of the lower third of the vagina, with or without extension onto pelvic sidewall, or hydronephrosis/non-functioning kidney, or spread to adjacent pelvic organs.
  - FIGO 2018 contains a new stage category (IIIC) with the presence of micrometastasis. FIGO 2018 IIIC is defined as involvement of pelvic and/or para-aortic lymph nodes (including micrometastases), irrespective of tumor size and extent

Appendix G: States with Regulations against Redirections in Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA
LA	Yes[≠]	For stage 4 advanced, metastatic cancer or associated conditions. [≠]Exception if clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy
MS	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial and HIM requests only** For stage 4 metastatic cancer and associated conditions
OK	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes^	For stage 4 advanced metastatic cancer, metastatic blood cancer and associated conditions ^ Exception if step therapy is AB-rated generic equivalent, interchangeable biological product, or biosimilar product to the equivalent brand drug
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pediatrics		
cHL, PMBCL, MSI-H or dMMR cancer, MCC, TMB-H cancer	2 mg/kg IV every 3 weeks up to 24 months	200 mg every 3 weeks
Melanoma	2 mg/kg IV every 3 weeks up to 12 months	200 mg every 3 weeks
Adults		
Melanoma	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
HNSCC	200 mg IV every 3 weeks OR 400 mg every 6 weeks for the following durations: up to 24 months* OR 6 weeks for neoadjuvant treatment** OR 1 year for adjuvant treatment*** **As single-agent therapy or in combination with chemotherapy* ***As single-agent therapy* ****In combination with RT with or without cisplatin, then continued as a single agent*	200 mg every 3 weeks OR 400 mg every 6 weeks
NSCLC	200 mg IV every 3 weeks OR 400 mg every 6 weeks for the following durations: up to 24 months* OR up to 12 months for adjuvant treatment** OR 12 weeks for neoadjuvant treatment*** followed by adjuvant treatment for 39 weeks** **As single-agent therapy or in combination with chemotherapy* ***As single-agent therapy* **** In combination with chemotherapy*	200 mg every 3 weeks OR 400 mg every 6 weeks
MPM, cHL, PMBCL, urothelial carcinoma, MSI-H or dMMR cancer (including endometrial carcinoma), gastric cancer, esophageal cancer, cervical cancer, HCC, BTC, MCC, TMB-H cancer, cSCC	200 mg IV every 3 weeks OR 400 mg every 6 weeks up to 24 months* **Esophageal cancer or gastric cancer: as single-agent therapy or in combination with chemotherapy* *For cervical cancer: as single-agent therapy or in combination with chemotherapy or CRT* *For urothelial carcinoma: as single-agent therapy or in combination with Padcev.* *For BTC, MPM: in combination with chemotherapy*	200 mg every 3 weeks OR 400 mg every 6 weeks
RCC (combination therapy)	200 mg IV every 3 weeks OR 400 mg every 6 weeks in combination with axitinib or lenvatinib up to 24 months	200 mg every 3 weeks OR 400 mg every 6 weeks

Indication	Dosing Regimen	Maximum Dose
RCC (monotherapy)	200 mg IV every 3 weeks OR 400 mg every 6 weeks for up to 12 months	200 mg every 3 weeks OR 400 mg every 6 weeks
Endometrial carcinoma (combination therapy)	200 mg IV every 3 weeks OR 400 mg every 6 weeks prior to carboplatin and paclitaxel when given on the same day or in combination with lenvatinib, up to 24 months	200 mg every 3 weeks OR 400 mg every 6 weeks
TNBC	200 mg IV every 3 weeks OR 400 mg every 6 weeks* for the following durations: • High-risk early-stage TNBC – neoadjuvant: 24 weeks • High-risk early-stage TNBC – adjuvant: 27 weeks • Locally recurrent unresectable metastatic TNBC: 24 months **In combination with chemotherapy for high-risk early-stage TNBC when used as neoadjuvant treatment and for locally recurrent unresectable or metastatic TNBC.*	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 2025. Available at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf. Accessed July 1, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at https://www.nccn.org/professionals/drug_compendium/content/. Accessed May 23, 2025.
3. 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. March 9, 2018;16(5):805-812. https://pubmed.ncbi.nlm.nih.gov/29523759/. Accessed April 24, 2025.

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
3Q 2021 annual review: RT4: criteria added for newly approved indications of 1) esophageal/GEJ junction carcinoma, 2) combo use for 1st line gastric or GEJ adenocarcinoma, 3) locally advanced cutaneous squamous cell carcinoma, and 4) high-risk early-stage TNBC; removed SCLC indication and criteria; updated FDA labeled indication for endometrial carcinoma to remove accelerated approval language and modified criteria to be consistent with FDA language; updated FDA labeled indication language for MSI-H/dMMR cancer; added Legacy WellCare with 12 month initial approval durations (WCG.CP.PHAR.322 to be retired); updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	05.11.21	08.21
RT4: criteria added for new FDA approved indication: RCC in combination with lenvatinib.	08.20.21	
RT4: updated FDA Approved Indication(s) section to reflect revised indication for metastatic urothelial carcinoma (removal of use in patients "who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test") – no change to criteria required.	09.15.21	
RT4: criteria added for new FDA approved indication: cervical cancer in combination with chemotherapy with or without bevacizumab.	10.19.21	
RT4: criteria added for new FDA approved indication: adjuvant treatment of RCC.	12.01.21	
RT4: for melanoma criteria added per updated prescribing information for pediatric extension in stage III disease and new indications for both adults and pediatrics for stage IIB and IIC; for RCC clarified maximum dosing for initial and continued approvals to distinguish length of therapy for 12 months in monotherapy and 24 months for combination therapy.	12.20.21	
RT4: removal of previously approved indication for usage as third-line monotherapy for PD-L1 positive gastric/GEJ cancer patients per updated prescribing information.	02.25.22	
3Q 2022 annual review: RT4: updated FDA Approved Indication(s) section to include newly approved indication for use as monotherapy for MSI-H or dMMR endometrial carcinoma (no change to criteria required); revisions per NCCN – melanoma: added requirement for use as a single agent or in combination with Lenvima or Yervoy; NSCLC: added requirement for no contraindications to PD-1/PD-L1 inhibitors, clarified criteria regarding disease mutation status (disease should be negative for actionable biomarkers and prior targeted therapy is now required only for ROS1 and EGFR S768I, L861Q, and/or G719X mutations), added pathway for use as single-agent continuation maintenance therapy if previously given first line as part	05.03.22	08.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
of a chemotherapy regimen; HNSCC: added pathway for combination use with docetaxel or gemcitabine; cHL: added pathway for combination use with GVD in adults; cSCC, HCC, PMBCL: added requirement for use as a single agent; urothelial carcinoma: added requirement for use as a single agent for locally advanced or metastatic disease in members who are ineligible for or have previously received platinum-containing chemotherapy; MSI-H/dMMR cancers: added additional cancers for which Keytruda may be used first line (ampullary adenocarcinoma, non-nasopharyngeal head and neck cancer, pancreatic adenocarcinoma), removed requirement for oxaliplatin contraindication for small bowel adenocarcinoma, added requirement for use as a single agent; RCC: added requirement for use as a single agent for adjuvant treatment; TMB-H cancer: added pathway for use as first-line for ampullary adenocarcinoma or pancreatic adenocarcinoma, added requirement for use as a single agent; off-label uses: added additional coverable cancers (adrenocortical carcinoma, alveolar soft part sarcoma, anaplastic large cell lymphoma, small cell lung cancer), added pathway for use as first line for thymic carcinoma, removed use for malignant pleural mesothelioma, updated mycosis fungoides to allow stage IIB, updated anal carcinoma to require no prior treatment with Keytruda or Opdivo, updated cancers where Keytruda is to be used only as subsequent therapy to require use as a single agent, updated extranodal NK/T-cell lymphoma to remove nasal type specification; revised legacy WellCare Medicaid initial approval durations from 12 months to 6 months to align with CNC Medicaid; references reviewed and updated.		
RT4: for endometrial carcinoma for use in combination with Lenvima, revised dMMR to pMMR per updated FDA approved indication. Template changes applied to other diagnoses/indications.	08.23.22	
RT4: added criteria for newly FDA approved indication of single-agent adjuvant therapy for NSCLC, added “as determined by an FDA-approved test” for MSI-H/dMMR cancer and microsatellite instability-high or mismatch repair deficient CRC, and revised “adult indications: additional dosing regimen” to apply only to adult cHL and PMBCL per updated PI; revised NSCLC criteria to include additional requirements related to mutation status per NCCN compendium; references reviewed and updated.	02.08.23	
RT4: added additional urothelial cancer indication in combination with enfortumab vedotin for patients ineligible for cisplatin-containing chemotherapy, and updated FDA approved indication for MSI-H/dMMR solid tumors to reflect full FDA approval per PI.	04.25.23	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2023 annual review: cHL, PMBCL, MSI-H/dMMR, MCC, TMB-H: adjusted pediatric age from 2 years to 6 months per PI/KEYNOTE-051; for Melanoma added option to be prescribed in combination with Mekinist and Trafinlar for disease with BRAF V600 activating mutation per NCCN; added endemic or classic Kaposi Sarcoma for adult off-label use and hypermutant tumor diffuse high-grade glioma for pediatric off-label use per NCNN; added criterion prescribed as single agent for Merkel cell carcinoma per NCCN; for HCC, added option for Stivarga; for pediatric PMBCL added option to be prescribed in combination with Adcetris; for endometrial carcinoma added option for combination with carboplatin and paclitaxel if disease is recurrent or stage III-IV tumor; references reviewed and updated.	05.16.23	08.23
RT4: updated FDA-approved indication for MCC to full FDA approval and added new indication of HER2-negative gastric/GEJ per PI; for NSCLC, criteria added for new FDA approved indication – "combination with platinum-containing chemotherapy as neoadjuvant therapy, then continued as single agent as adjuvant treatment after surgery for patients with tumors ≥ 4 cm or node positive" and option for disease to be resectable or resected per updated PI; added criteria for newly approved FDA indication for BTC per PI and NCCN; for gastric/esophageal/GEJ cancer, clarified specific uses per updated PI, including requirement that tumor must be HER2-positive and express PD-L1 (CPS ≥ 1) when prescribed in combination use with trastuzumab for gastric/GEJ adenocarcinoma; for MSI-H/dMMR, added gastric or GEJ cancer as cancer type that can be prescribed as first line or subsequent therapy and added option to prescribe in combination with platinum- and fluoropyrimidine-based chemotherapy for gastric or GEJ cancer per NCCN; for urothelial cancer in combination with Padcev, updated FDA-approved indication to full approval and removed requirement for cisplatin ineligibility per updated PI.	12.19.23	
RT4: for cervical cancer, criteria added for new FDA indication for usage in combination with CRT with FIGO 2014 Stage III-IVA cancer.	01.17.24	
RT4: updated FDA-approved indication section for HCC to full approval with update from those "who have previously been treated with sorafenib" to "secondary to hepatitis B who have received prior systemic therapy other than a PD-1/PD-L1-containing regimen" per PI; for HCC, added option for prior use of Cabometyx and added option to be prescribed as first-line treatment per NCCN.	02.13.24	
3Q 2024 annual review: for cHL, added option to be prescribed with ICE and added pathway for palliative therapy (previously had after	07.02.24	08.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
hematopoietic stem cell transplant, which falls under palliative therapy) per NCCN; for UC, added pathway to be prescribed as single agent and member has previously received other chemotherapy (previously only allowed post-platinum chemotherapy); for HCC, removed disease is classified as Child-Pugh Class A; for BTC, added option for resected gross residual (R2) disease and removed combination with Lenvima per NCCN; for endometrial carcinoma, clarified continued as a single agent for maintenance therapy when prescribed in combination with carboplatin and paclitaxel; for NCCN recommended uses (off-label): expanded to stage IB for mycosis fungoides, for prescribed as first-line or subsequent therapy - added metastatic anaplastic carcinoma, anaplastic sarcoma, and vaginal cancer, for prescribed as single-agent subsequent therapy – added soft tissue sarcoma subtypes, added option for Keytruda to be prescribed in combination with cyclophosphamide and bevacizumab for platinum-resistant persistent ovarian cancer, fallopian tube cancer, and primary peritoneal cancer per NCCN; for continuation requests, added criterion for maximum duration of therapy (previously was included within requests for dose increase criterion); updated appendix E; references reviewed and updated. RT4: added new FDA approved indication for endometrial cancer in combination with carboplatin and paclitaxel followed by Keytruda as a single agent per PI.		
RT4: added new FDA approved indication for MPM.	09.30.24	
RT4: updated FDA Approved Indication section for EC in combination with lenvatinib to require FDA-approved testing for both MSI-H and pMMR (previously required for pMMR only) per PI.	02.13.25	
Per March SDC, for HNSCC, added redirection for nasopharyngeal carcinoma to Loqtorzi; added Appendix G to include states with regulations against redirections in cancer. RT4: updated FDA Approved Indication(s) section for first-line treatment of adults with locally advanced unresectable or metastatic HER2-positive gastric or GEJ adenocarcinoma in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy whose tumors express PD-L1 (CPS ≥ 1) from accelerated approval to full approval per PI; for gastric cancer, esophageal cancer, or GEJ cancer, added option to bypass disease is unresectable, locally advanced, recurrent, or metastatic if member is planned for esophagectomy per NCCN. Added step therapy bypass for IL HIM per IL HB 5395.	03.31.25	05.25
3Q 2025 annual review: for NSCLC, updated targeted therapies for EGFR exon 19 deletion, L858R, and ROS1 rearrangement positive disease; for HNSCC added option to be prescribed in combination	07.01.25	08.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
with Erbitux as first-line therapy or subsequent-line therapy; for cHL, added option to be prescribed in combination with decitabine and vorinostat, for post-allogenic hematopoietic cell transplant or post autologous stem cell rescue, and members not candidate for anthracycline therapy and revised for relapsed disease for both adults and pediatrics after ≥ 1 line of systemic therapy (previously ≥ 2 lines of systemic therapy for pediatrics); for UC, added option to be prescribed in combination with Inlyta or Lenvima, usage for relapsed disease, and prescribed as a single agent for adjuvant therapy; for cervical cancer, added FIGO 2018 stage III-IVA in combination with CRT and added option to be prescribed in combination with Tivdak for tumors expressing PD-L1 and has not received prior immune-oncology therapy, recurrent or metastatic disease, and disease as progressed on or after ≥ 1 line of systemic therapy; for HCC, removed specific treatment regimens member has had disease progression following from and revise to prescribed as subsequent line therapy; for BTC, added option for disease is resectable locoregionally advanced and prescribed as neoadjuvant therapy for gallbladder cancer; for TNBC, added option to be prescribed as preoperative systemic therapy in combination with carboplatin and docetaxel; added off-label usage for central nervous (CNS) cancer, thyroid carcinoma, peritoneal mesothelioma, penile cancer; for mycosis fungoides, revised stage to Stage IA – III; for thymic carcinoma, removed metastatic or unresectable requirement; RT4: updated FDA Approved Indication(s) section and criteria to reflect revised indication that limits use to tumors expressing PD-L1 (CPS ≥ 1) for esophageal or GEJ carcinoma in combination with chemotherapy and HER2-negative gastric or GEJ adenocarcinoma as first-line therapy in combination with chemotherapy per updated PI (previously approved regardless of PD-L1 status); RT4: updated FDA Approved Indications(s) section for cervical cancer to clarify FIGO 2014 Stage III-IVA per updated PI; updated Appendix E with addition of soft tissue sarcoma as an example for MSI-H solid tumors and small bowel adenocarcinoma for TMB-H solid tumors; updated Appendix G with revised language and exception for Tennessee; references reviewed and updated. Per June SDC: added redirection to Tevimbra for HER2-negative gastric or GEJ adenocarcinoma and esophageal carcinoma or GEJ squamous cell carcinoma. RT4: added new FDA approved indication for usage in the neoadjuvant/adjuvant setting for locally advanced HNSCC.		

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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.