STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Keytruda (pembrolizumab)
PAM-008

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	04/30/2015
Revision Number:	7	**Last Rev Date:**	07/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	07/18/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	04/28/2020

Overview

Medication:[1]	pembrolizumab
Brand Name:	Keytruda®
Pharmacologic Category:	Antineoplastic; programmed death receptor-1 (PD-1)-blocking antibody
FDA-Approved Indications:	See list of FDA-approved indications on following pages
How Supplied:	• Single-dose vial: 100 mg/4 mL (25 mg/mL) solution • Supplied in a carton containing 1 or 2 vials
Dosage and Administration:	• Intravenous (IV) infusion • Dosage is indication specific (see Appendix A)
Benefit Category:	Medical

Abbreviations/Acronyms

- ALK: anaplastic lymphoma kinase
- BCG: Bacillus Calmette-Guerin
- 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: U.S. Food and Drug Administration
- FIGO: International Federation of Gynecology and Obstetrics
- GEJ: gastroesophageal junction
- 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
- ORR: objective response rate
- OS: overall survival
- PD-1: programmed death protein 1
- PD-L1: programmed death-ligand 1
- PFS: progression-free survival
- PMBCL: primary mediastinal large B-cell lymphoma
- pMMR: mismatch repair proficient
- RCC: renal cell carcinoma
- RFS: recurrence-free survival
- ROS1: ROS proto-oncogene 1
- TMB-H: tumor mutational burden-high
- TNBC: triple-negative breast cancer
- TPS: tumor proportion score
- TTP: time to progression

Descriptive Narrative

Binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells, inhibits T cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumors and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumors. Keytruda® (pembrolizumab) is a monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. In syngeneic mouse tumor models, blocking PD-1 activity resulted in decreased tumor growth.

FDA-Approved Indications

Keytruda® is indicated:

1. **Melanoma**
   a. For the treatment of patients with unresectable or metastatic melanoma.
   b. For the adjuvant treatment of adult and pediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma following complete resection.

2. **Non-Small Cell Lung Cancer (NSCLC)**
   a. In combination with pemetrexed and platinum chemotherapy: for the first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations.
   b. In combination with carboplatin and either paclitaxel or paclitaxel protein-bound: for the first-line treatment of patients with metastatic squamous NSCLC.
   c. As a single agent: for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
      i. Stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
      ii. metastatic.
   d. As a single agent: for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda®.
   e. In combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery: for the treatment of patients with resectable (tumors ≥ 4 cm or node positive) NSCLC.
      ► **NEW** indication (FDA-approved 10/16/2023)
   f. As a single agent: is indicated as adjuvant treatment following resection and platinum-based chemotherapy for adult patients with Stage IB (T2a ≥4 cm), II, or IIIA NSCLC.

3. Head and Neck Squamous Cell Cancer (HNSCC)

a. In combination with platinum and fluorouracil: for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC.
b. As a single agent: for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test.
c. As a single agent: for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

4. Classical Hodgkin Lymphoma (cHL)

a. For the treatment of adult patients with relapsed or refractory cHL.
b. For the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.

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

a. For the treatment of adult and pediatric patients with refractory PMBCL, or who have relapsed after 2 or more prior lines of therapy.
   - ► Limitations of Use: Keytruda® is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

6. Urothelial Carcinoma

a. In combination with enfortumab vedotin: for the treatment of adult patients with locally advanced or metastatic urothelial cancer.
   - ► **MODIFIED** indication and **CONVERTED** from accelerated approval to regular approval (FDA-approved 12/15/2023)
b. As a single agent: for the treatment of patients with locally advanced or metastatic urothelial carcinoma:
   i. who are not eligible for any platinum-containing chemotherapy, or
   ii. who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
c. 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.

7. Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Cancer

a. 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.

8. Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer

a. For the treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC) as determined by an FDA-approved test.

9. Gastric Cancer

a. In combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy: for the first-line treatment of adults 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.
   - ► **MODIFIED** indication (FDA-approved 11/16/2023)
   - ► Accelerated Approval: This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval of this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

b. 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 gastroesophageal junction (GEJ) adenocarcinoma.
   - ► **NEW** indication (FDA-approved 11/7/2023)

10. Esophageal Cancer

a. For the treatment of patients with locally advanced or metastatic esophageal or gastro-esophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either:
   i. in combination with platinum- and fluoropyrimidine-based chemotherapy, or
   ii. as a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1 (CPS ≥10) as determined by an FDA-approved test.

11. Cervical Cancer

a. In combination with chemoradiotherapy [CRT]: for the treatment of patients with FIGO 2014 Stage III-IVA cervical cancer. *(FIGO = International Federation of Gynecology and Obstetrics)*
   - ► **NEW** indication (FDA-approved 1/12/2024)

b. 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.

c. As a single agent: for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.

12. Hepatocellular Carcinoma (HCC)

a. For the treatment of patients with HCC secondary to hepatis B who have received prior systemic therapy other than a PD-1/PD-L1-containing regimen.
   - ► **MODIFIED** indication and **CONVERTED** to regular approval (FDA-approved 1/25/2024)

13. Biliary Tract Cancer (BTC)

a. In combination with gemcitabine and cisplatin: for the treatment of patients with locally advanced unresectable or metastatic BTC.
   - ► **NEW** indication (FDA-approved 10/31/2023)

14. Merkel Cell Carcinoma (MCC)

a. For the treatment of adult and pediatric patients with recurrent locally advanced or metastatic MCC.
   - ► **CONVERTED** from accelerated to regular approval (FDA-approved 10/12/2023).

15. Renal Cell Carcinoma (RCC)

a. In combination with axitinib: for first-line treatment of adult patients with advanced RCC.
b. In combination with lenvatinib: for first-line treatment of adult patients with advanced RCC.
c. For the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions.

16. Endometrial Carcinoma

a. In combination with lenvatinib: for the treatment of patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.
b. As a single agent: for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

17. Tumor Mutational Burden-High Cancer (TMB-H)

a. For the treatment of adult and pediatric patients with unresectable or metastatic 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.
   - ► Accelerated Approval: 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.
   - ► Limitations of Use: The safety and effectiveness of Keytruda® in pediatric patients with TMB-H central nervous system cancers have not been established.

18. Cutaneous Squamous Cell Carcinoma (cSCC)

a. For the treatment of patients with recurrent or metastatic cSCC or locally advanced cSCC that is not curable by surgery or radiation.

19. Triple-Negative Breast Cancer (TNBC)

a. 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.
b. 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.

20. Adult Classical Hodgkin Lymphoma and Adult Primary Mediastinal Large B-Cell Lymphoma: Additional Dosing Regimen of 400 mg Every 6 Weeks

a. Keytruda® is indicated for use at an additional recommended dosage of 400 mg every 6 weeks for classical Hodgkin lymphoma and primary mediastinal large B-cell lymphoma in adults.
   - ► Accelerated Approval: 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 dosage may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[2]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from: [3]

- Melanoma: Cutaneous (Version 2.2024 – March 3, 2024)
- Non-Small Cell Lung Cancer (Version 5.2024 – April 23, 2024)
- Head and Neck Cancers (Version 4.2024 – May 1, 2024)
- Hodgkin Lymphoma (Version 3.2024 – March 18, 2024)
- Pediatric Hodgkin Lymphoma (Version 1.2024 – May 14, 2024)
- B-Cell Lymphomas (Version 2.2024 – April 30, 2024)
- Bladder Cancer (Version 4.2024 – May 9, 2024)
- Colon Cancer (Version 3.2024 – May 24, 2024)
- Gastric Cancer (Version 2.2024 – May 29, 2024)
- Esophageal and Esophagogastric Junction Cancers (Version 3.2024 – April 26, 2024)
- Cervical Cancer (Version 3.2024 – May 6, 2024)
- Hepatocellular Carcinoma (Version 1.2024 – April 9, 2024)
- Biliary Tract Cancers (Version 2.2024 – April 19, 2024)
- Merkel Cell Carcinoma (Version 1.2024 – November 22, 2023)
- Kidney Cancer (Version 4.2024 – May 30, 2024)
- Uterine Neoplasms (Version 2.2024 – March 6, 2024)
- Squamous Cell Skin Cancer (Version 1.2024 – November 9, 2023)
- Breast Cancer (Version 2.2024 – March 11, 2024)

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Tools for Assessment of Patient Functional Levels

The Karnofsky Performance Status and the Eastern Cooperative Oncology Group Performance Status are widely used methods to assess the functional status of a patient. The Karnofsky Status describes a patient's functional status as a comprehensive 11-point scale correlating to percentage values ranging from 100 percent (no evidence of disease, no symptoms) to 0 percent (death). The Eastern Cooperative Oncology Group Performance Status describes a patient's functional status using a scale which ranges from 0 (healthy, no pain) to 5 (death).

For years, these two assessment methodologies have been important tools in clinical practice. In clinical trials, they are used as selection criteria (similar to processes for selection using age or gender) and for the stratification of subgroups in test patient cohorts.[4] Both are used by doctors and researchers to assess how a patient's disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis.[5]

A third functional assessment tool, the Lansky Play-Performance Scale, may be utilized to assess the functional status of patients younger than 16 years of age[6] (the Karnofsky Performance Status is used in patients 16 years of age and older).

Performance Status Assessments					
Eastern Cooperative Oncology Group Performance Status		Karnofsky Performance Status		Lansky Play-Performance Scale	
Score	Description	Score	Description	Score	Description
0	Fully active, able to carry on all pre-disease performance without restriction.	100	Normal, no complaints, no evidence of disease.	100	Fully active, normal.
		90	Able to carry on normal activity, minor signs or symptoms of disease.	90	Minor restrictions in physically strenuous activity.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (light housework, office work).	80	Normal activity with effort, some signs or symptoms of disease.	80	Active, but tires more quickly.
		70	Cares for self, unable to carry on normal activity or do active work.	70	Both greater restriction of, and less time spent in, play activity.
2	Ambulatory and capable of all self-care but unable to carry out any work. Activities; up and about more than 50% of waking hours.	60	Requires occasional assistance but is able to care for most of his/her needs.	60	Up and around, but minimal active play; keeps busy with quieter activities.
		50	Requires considerable assistance and frequent medical care.	50	Gets dressed but lies around much of the day; no active play; able to participate in all quiet play and activities.
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.	40	Disabled, requires special care and assistance.	40	Mostly in bed, participates in quiet activities.
		30	Severely disabled, hospitalization indicated. Death not imminent.	30	In bed, needs assistance even for quiet play.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.	20	Very sick, hospitalization indicated. Death not imminent.	20	Often sleeping, play entirely limited to very passive activities.
		10	Moribund, fatal processes progressing rapidly.	10	No play, does not get out of bed.
5	Dead.	0	Dead.	0	Dead.

Criteria

Prior authorization is required for all indications.

All FDA-Approved Indications

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Prescribed by, or in consultation with, an oncologist (unless noted otherwise); **AND**
2. Member is not receiving therapy for a chronic condition, such as an autoimmune disease, which requires systemic steroids or immunosuppressive agents; **AND**
3. Member does not have an active infection requiring systemic therapy; **AND**
4. The regimen prescribed is within FDA-approved labeling. If dose or schedule exceeds the FDA-approved labeling, therapy regimen (including dosage) must be supported by clinical practice guidelines (i.e., must be recommended in the NCCN Clinical Practice Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen or dosage prescribed does not align with FDA-approved labeling; **AND**
5. All indication-specific criteria are also met (listed following this section).

1. Melanoma

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of melanoma; **AND**
3. Member meets one of the following (a, b, or c):
    a. 6 months through 16 years of age and has a current Lansky Play Status ≥ 50; or
    b. 17 years of age and has a current Karnofsky Performance Status ≥ 50; or
    c. 18 years of age or older and has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
4. Keytruda® is used as monotherapy, and is either (a or b):
    a. Used in the treatment of unresectable or metastatic melanoma; **OR**
    b. Used as adjuvant therapy in Stage IIB, IIC, or III melanoma following complete resection and member is 12 years of age or older.

2. Non-Small Cell Lung Cancer (NSCLC)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of non-small cell lung cancer (NSCLC); **AND**
3. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
4. Member is 18 years of age or older; **AND**
5. Keytruda® is prescribed in **ONE** of the following ways (a, b, c, d, e, or f):
    a. In combination with pemetrexed* and platinum chemotherapy as a first-line treatment for metastatic nonsquamous NSCLC, with no EGFR‡ or ALK‡ genomic tumor aberrations; **OR**
    b. In combination with carboplatin and either paclitaxel or paclitaxel protein-bound as first-line treatment for metastatic squamous NSCLC; **OR**
    c. As monotherapy for first-line treatment of NSCLC expressing PD-L1‡ [tumor proportion score (TPS) ≥1 percent], with no EGFR‡ or ALK‡ genomic tumor aberrations, and is either stage III (and member is not a candidate for surgical resection or definitive chemoradiation) or is metastatic; **OR**
    d. As monotherapy for metastatic NSCLC in a member whose tumors express PD-L1‡ (TPS ≥1 %) and with disease progression on or after platinum-containing therapy§; **OR**
    e. In combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery, for patients with resectable (tumors ≥ 4 cm or node positive) NSCLC; **OR**
    f. As monotherapy for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with Stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC.

* Pemetrexed (Alimta®) may require a separate prior authorization.

‡ Genomic testing for epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) tumor aberrations or for programmed death-ligand 1 (PD-L1) expression may require a separate prior authorization.

§ If member has EGFR‡ or ALK‡ genomic tumor aberrations, should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda®

3. Head and Neck Squamous Cell Cancer (HNSCC)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of head and neck squamous cell cancer (HNSCC); **AND**
3. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
4. Member is 18 years of age or older; **AND**
5. Keytruda® is prescribed in **ONE** of the following ways (a, b, or c):
    a. In combination with platinum and fluorouracil as first-line treatment of metastatic or unresectable, recurrent HNSCC; **OR**
    b. As monotherapy for first-line treatment of metastatic or unresectable, recurrent HNSCC with tumors expressing PD-L1[≠] [combined positive score (CPS) ≥ 1]; **OR**
    c. As monotherapy for recurrent or metastatic HNSCC in a member with disease progression on or after platinum-containing chemotherapy.

[≠] Genomic testing for programmed death-ligand 1 (PD-L1) expression may require a separate prior authorization.

4. Classical Hodgkin Lymphoma (cHL)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of classical Hodgkin lymphoma (cHL); **AND**
3. Member meets one of the following (a, b, or c):
    a. 6 months through 16 years of age and has a current Lansky Play Status ≥ 50; or
    b. 17 years of age and has a current Karnofsky Performance Status ≥ 50; or
    c. 18 years of age or older and has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
4. Keytruda® is prescribed in **ONE** of the following ways (a or b):
    a. For relapsed or refractory cHL in a member who is 18 years of age or older; **OR**
    b. Refractory cHL, or cHL that has relapsed after two or more lines of therapy, in a member who is 2 years of age or older.

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

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of primary mediastinal large B-cell lymphoma (PMBCL); **AND**
3. Member is 2 years of age or older; **AND**
4. Member has refractory PMBCL or has relapsed after two or more prior lines of therapy; **AND**
5. Member meets one of the following (a, b, or c):
    a. 2 years through 16 years of age and has a current Lansky Play Status ≥ 50; or
    b. 17 years of age and has a current Karnofsky Performance Status ≥ 50; or
    c. 18 years of age or older and has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
6. Keytruda® is prescribed as monotherapy.

Keytruda® is **NOT** considered medically necessary in members who require urgent cytoreductive therapy.

6. Urothelial Carcinoma

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of urothelial carcinoma; **AND**
3. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2; **AND**
4. Member is 18 years of age or older; **AND**
5. Prescribed by, or in consultation with, an oncologist or urologist; **AND**
6. Keytruda is prescribed in **ONE** of the following ways (a, b, or c):
    a. In combination with enfortumab vedotin (Padcev®) for treatment of locally advanced or metastatic urothelial cancer; **OR**
    b. As monotherapy for the treatment of locally advanced or metastatic urothelial carcinoma in a member who either is not eligible for any platinum-containing therapy or who has had disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; **OR**
    c. As monotherapy for the treatment of a member who has Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors and is either ineligible for, or has elected not to undergo, cystectomy.

7. Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient Cancer (dMMR)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of unresectable or metastatic solid tumors classified as MSI-H [≠] or dMMR [≠] (indicative of MMR gene mutation or loss of expression); **AND**
3. Member has progressed following prior treatment and has no satisfactory alternative treatment options; **AND**
4. Member meets one of the following (a, b, or c):
    a. 6 months through 16 years of age and has a current Lansky Play Status ≥ 50; or
    b. 17 years of age and has a current Karnofsky Performance Status ≥ 50; or
    c. 18 years of age or older and has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
5. Keytruda® is prescribed as monotherapy.

[≠] Genomic testing for microsatellite instability-high (MSI-H) and mismatch repair deficient (dMMR) may require a separate prior authorization.

8. Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient Cancer (dMMR) Colorectal Cancer (CRC)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of unresectable or metastatic colorectal cancer (CRC); **AND**
3. Tumor status is classified as MSI-H [≠] or dMMR [≠]; **AND**
4. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
5. Keytruda® is prescribed as monotherapy in one of two ways (a or b):
    a. As first-line therapy; **OR**
    b. As subsequent therapy (if member who has not received prior immunotherapy).

[≠] Genomic testing for microsatellite instability-high (MSI-H) and mismatch repair deficient (dMMR) may require a separate prior authorization.

9. Gastric Cancer

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of gastric or gastroesophageal junction (GEJ) adenocarcinoma; **AND**
3. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
4. Member is 18 years of age or older; **AND**
5. Keytruda® is prescribed in ONE of the following ways (a or b):
    a. In combination with trastuzumab*, fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of a member with locally advanced unresectable or metastatic HER2-positive[≠] gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1); **OR**
    b. In combination with fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of a member with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma.

[≠] Genomic testing for human epidermal growth factor receptor 2 (HER2) may require a separate prior authorization.
* Trastuzumab may require separate prior authorization.

10. Esophageal Cancer

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of esophageal or gastroesophageal junction (GEJ) carcinoma (tumors with epicenter 1 to 5 centimeters above the GEJ); **AND**
3. Disease is locally advanced or metastatic, and is not amenable to surgical resection or definitive chemoradiation; **AND**
4. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
5. Member is 18 years of age or older; **AND**
6. Keytruda® is prescribed in **ONE** of two ways (a or b):
    a. In combination with platinum- and fluoropyrimidine-based chemotherapy; **OR**
    b. As monotherapy after one or more prior lines of systemic therapy for tumor(s) of squamous cell histology that express PD-L1[≠] [combined positive score (CPS) ≥10].

[≠] Genomic testing for programmed death-ligand 1 (PD-L1) expression may require a separate prior authorization.

11. Cervical Cancer

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of cervical cancer; **AND**
3. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
4. Member is 18 years of age or older; **AND**
5. Keytruda® is prescribed in **ONE** of the following ways (a, b, or c):
    a. In combination with chemoradiotherapy (CRT) for the treatment of patients with FIGO 2014 Stage III-IVA cervical cancer; **OR**
    b. In combination with chemotherapy, with or without bevacizumab*, for persistent, recurrent, or metastatic cervical cancer with tumors which express PD-L1[‡] [Combined positive score (CPS) ≥1]; **OR**
    c. As monotherapy for recurrent or metastatic cervical cancer with tumors which express PD-L1[‡] (CPS ≥ 1) and member has disease progression on or after chemotherapy.

FIGO = International Federation of Gynecology and Obstetrics (Federation Internationale de Gynecologie et d'Obstetrique)

* Bevacizumab may require separate prior authorization.

[‡] Genomic testing for programmed death-ligand 1 (PD-L1) expression may require a separate prior authorization.

12. Hepatocellular Carcinoma (HCC)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of hepatocellular carcinoma (HCC) secondary to hepatitis B; **AND**
3. Member has received prior systemic therapy other than a PD-1/PD-L1-containing regimen; **AND**
4. Member is 18 years of age or older; **AND**
5. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
6. Keytruda® is prescribed as monotherapy.

13. Biliary Tract Cancer (BTC)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of biliary tract cancer (BTC); **AND**
3. Disease is locally advanced unresectable or metastatic; **AND**
4. Member is 18 years of age or older; **AND**
5. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
6. Keytruda® is prescribed in combination with gemcitabine and cisplatin.

14. Merkel Cell Carcinoma (MCC)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of Merkel cell carcinoma (MCC): **AND**
3. Disease is recurrent locally advanced or metastatic; **AND**
4. Member meets one of the following (a, b, or c):
    a. 6 months through 16 years of age and has a current Lansky Play Status ≥ 50; or
    b. 17 years of age and has a current Karnofsky Performance Status ≥ 50; or
    c. 18 years of age or older and has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1.
5. Keytruda® is prescribed as monotherapy.

15. Renal Cell Carcinoma (RCC)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of renal cell carcinoma (RCC); **AND**
3. Member meets **ONE** of the following:
    a. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 1; **OR**
    b. Karnofsky Performance Status ≥ 70; **AND**
4. Member is 18 years of age or older; **AND**
5. Keytruda® is prescribed in **ONE** of the following ways (a, b, c, or d):
    a. In combination with axitinib* as a first-line treatment for advanced RCC; **OR**
    b. In combination with lenvatinib* as a first-line treatment of advanced RCC; **OR**
    c. As a single-agent adjuvant treatment for RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions; **OR**
    d. As monotherapy for relapsed or stage IV disease with non-clear cell histology *(NCCN 2A)*.

* Axitinib and lenvatinib may require a separate pharmacy prior authorization (see Iowa Medicaid PDL for more information).

16. Endometrial Carcinoma

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of endometrial carcinoma; **AND**
3. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
4. Member is 18 years of age or older; **AND**
5. Member has had disease progression following prior systemic therapy; **AND**
6. Member is not a candidate for curative surgery or radiation; **AND**
7. Keytruda® is prescribed in **ONE** of the two ways (a or b):
    a. In combination with lenvatinib* and carcinoma **is not** MSI-H [≠] or dMMR [≠]; **OR**
    b. As monotherapy and carcinoma **is** MSI-H[≠] or dMMR[≠].

[≠] Genomic testing for microsatellite instability-high (MSI-H) and mismatch repair deficient (dMMR) may require a separate prior authorization.

* Lenvatinib may require a separate pharmacy prior authorization (see Iowa Medicaid PDL for more information).

17. Tumor Mutational Burden-High Cancer (TMB-H)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of an unresectable or metastatic solid tumor; **AND**
3. Member has high tumor mutational burden (TMB-H) [≠] solid tumors, [≥ 10 mutations/megabase (mut/Mb)]; **AND**
4. Member has disease progression following prior treatment and has no satisfactory alternative treatment options; **AND**
5. Member meets one of the following (a, b, or c):
    a. 6 months through 16 years of age and has a current Lansky Play Status ≥ 50; or
    b. 17 years of age and has a Karnofsky Performance Status ≥ 50; or
    c. 18 years of age or older and has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
6. Keytruda® is prescribed as monotherapy.

[≠] Genomic testing for tumor mutational burden-high cancer (TMB) may require a separate prior authorization.

18. Cutaneous Squamous Cell Carcinoma (cSCC)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of cutaneous squamous cell carcinoma (cSCC); **AND**
3. Disease is (both a and b):
    a. Recurrent cSCC, metastatic cSCC ,or locally advanced cSCC; **AND**
    b. and Is not curable by surgery or radiation; **AND**
4. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
5. Member is 18 years of age or older; **AND**
6. Keytruda® is prescribed as monotherapy.

19. Triple-Negative Breast Cancer (TNBC)

Keytruda® is considered medically necessary when **ALL** of the following are met:

1. Criteria listed in "All Indications" section is met; **AND**
2. Confirmed diagnosis of triple-negative breast cancer (TNBC)*; **AND**
3. Member has a current Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
4. Member is 18 years of age or older; **AND**
5. Keytruda® is prescribed in **ONE** of the two following ways (a or b):
    a. In combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant therapy after surgery (for disease which is high-risk early stage); **OR**
    b. In combination with chemotherapy for disease which is locally recurrent unresectable or metastatic and tumor expresses PD-L1≠ [combined positive score (CPS) ≥10].

* Triple-negative breast cancer (TNBC) is estrogen receptor-negative (ER-negative), progesterone receptor-negative (PR-negative), and human epidermal growth factor receptor 2-negative (HER2-negative).
≠ Genomic testing for programmed death-ligand 1 (PD-L1) expression may require a separate prior authorization.

Criteria for Continuation of Therapy

Keytruda® is considered medically necessary for continuation of therapy (for all indications listed above) when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit and/or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist (unless otherwise noted in initial criteria); **AND**
4. The regimen prescribed is within the FDA-approved labeling. If dose or schedule exceeds the FDA-approved labeling, therapy regimen (including dosage) must be supported by clinical practice guidelines (i.e., must be recommended in the NCCN Clinical Practice Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen or dosing does not align with FDA-approved labeling; **AND**
5. Request does not exceed the approval duration or quantity limits outlined for each indication in the "Approval Duration and Quantity Limits" section.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorizations
Approval Duration	6 months	Up to 6 months per authorization (not to exceed maximum duration of therapy as indicated in FDA-approved labeling).
Quantity Limits	Not to exceed FDA-approved dosing (see Appendix A)	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9271	Injection, pembrolizumab, 1 mg.

ICD-10	Description
C4A.0	Merkel cell carcinoma of lip
C4A.1	Merkel cell carcinoma of eyelid, including canthus
C4A.11	Merkel cell carcinoma of right eyelid, including canthus
C4A.12	Merkel cell carcinoma of left eyelid, including canthus
C4A.2	Merkel cell carcinoma of ear and external auricular canal
C4A.3	Merkel cell carcinoma of other and unspecified parts of face
C4A.4	Merkel cell carcinoma of scalp and neck
C4A.5	Merkel cell carcinoma of trunk
C4A.6	Merkel cell carcinoma of upper limb, including shoulder
C4A.7	Merkel cell carcinoma of lower limb, including hip
C4A.8	Merkel cell carcinoma of overlapping sites
C4A.9	Merkel cell carcinoma, unspecified
C00	Malignant neoplasm of lip
C01	Malignant neoplasm of base of tongue
C02	Malignant neoplasm of other and unspecified parts of tongue
C03	Malignant neoplasm of gum
C04	Malignant neoplasm of floor of mouth
C05	Malignant neoplasm of palate
C06	Malignant neoplasm of other and unspecified parts of mouth
C09	Malignant neoplasm of tonsil
C10	Malignant neoplasm of oropharynx
C12	Malignant neoplasm of pyriform sinus
C13	Malignant neoplasm of hypopharynx
C14	Malignant neoplasm of other and ill-defined sites in the lip, oral cavity, and pharynx
C15	Malignant neoplasm of esophagus
C16	Malignant neoplasm of stomach
C18	Malignant neoplasm of colon
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21	Malignant neoplasm of anus and anal canal
C22	Malignant neoplasm of liver and intrahepatic bile ducts
C22.1	Intrahepatic bile duct carcinoma
C23	Malignant neoplasm of gall bladder
C24	Malignant neoplasm of other and unspecified parts of biliary tract
C30	Malignant neoplasm of nasal cavity and middle ear
C31	Malignant neoplasm of accessory sinuses
C32	Malignant neoplasm of larynx
C33	Malignant neoplasm of trachea
C34	Malignant neoplasm of bronchus and lung
C43	Malignant melanoma of skin
C44	Other and unspecified malignant neoplasm of skin
C44.12	Squamous cell carcinoma of skin of eyelid, including canthus

ICD-10	Description
C44.22	Squamous cell carcinoma of skin and ear and external auricular canal
C44.32	Squamous cell carcinoma of skin and other unspecified parts of face
C44.4	Other and unspecified malignant neoplasm of skin of scalp and neck
C44.52	Squamous cell carcinoma of skin of trunk
C44.62	Squamous cell carcinoma of skin of upper limb, including shoulder
C44.72	Squamous cell carcinoma of skin of lower limb, including hip
C44.8	Other and unspecified malignant neoplasm of overlapping sites of skin
C44.9	Other and unspecified malignant neoplasm of skin, unspecified
C50.01	Malignant neoplasm of nipple and areola, female
C50.02	Malignant neoplasm of nipple and areola, male
C50.11	Malignant neoplasm of central portion of breast, female
C50.12	Malignant neoplasm of central portion of breast, male
C50.21	Malignant neoplasm of upper-inner quadrant of breast, female
C50.22	Malignant neoplasm of upper-inner quadrant of breast, male
C50.31	Malignant neoplasm of lower-inner quadrant of breast, female
C50.32	Malignant neoplasm of lower-inner quadrant of breast, male
C50.41	Malignant neoplasm of upper-outer quadrant of breast, female
C50.42	Malignant neoplasm of upper-outer quadrant of breast, male
C50.51	Malignant neoplasm of lower-outer quadrant of breast, female
C50.52	Malignant neoplasm of lower-outer quadrant of breast, male
C50.61	Malignant neoplasm of axillary tail of breast, female
C50.62	Malignant neoplasm of axillary tail of breast, male
C50.81	Malignant neoplasm of overlapping sites of breast, female
C50.82	Malignant neoplasm of overlapping sites of breast, male
C50.91	Malignant neoplasm of breast of unspecified site, female
C50.92	Malignant neoplasm of breast of unspecified site, male
C51	Malignant neoplasm of vulva
C53	Malignant neoplasm of cervix uteri
C54	Malignant neoplasm of corpus uteri
C55	Malignant neoplasm of uterus, part unspecified
C57	Malignant neoplasm of other and unspecified female genital organs
C60	Malignant neoplasm of penis
C63	Malignant neoplasm of other and unspecified male genital organs
C64	Malignant neoplasm of kidney, except renal pelvis
C65	Malignant neoplasm of renal pelvis
C66	Malignant neoplasm of ureter
C67	Malignant neoplasm of bladder
C68	Malignant neoplasm of other and unspecified urinary organs
C76.0	Malignant neoplasm of head, face, and neck (other and ill-defined sites)
C81	Hodgkin lymphoma
C85	Other specified and unspecified types of non-Hodgkin lymphoma

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
00006-3026-02	Merck Sharp & Dohme Corp.	1 mg	1	EA	100
00006-3026-04	Merck Sharp & Dohme Corp.	1 mg	1	EA	200

Appendix A: Dosing (per indication)

Abbreviations/Acronyms

- ALK: anaplastic lymphoma kinase
- BCG: Bacillus Calmette-Guerin
- 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: U.S. Food and Drug Administration
- FIGO: International Federation of Gynecology and Obstetrics
- GEJ: gastroesophageal junction
- 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
- ORR: objective response rate
- OS: overall survival
- PD-1: programmed death protein 1
- PD-L1: programmed death-ligand 1
- PFS: progression-free survival
- PMBCL: primary mediastinal large B-cell lymphoma
- pMMR: mismatch repair proficient
- RCC: renal cell carcinoma
- RFS: recurrence-free survival
- ROS1: ROS proto-oncogene 1
- TMB-H: tumor mutational burden-high
- TNBC: triple-negative breast cancer
- TPS: tumor proportion score
- TTP: time to progression

MONOTHERAPY		
Indication	Recommended Dosage	Duration of Treatment
Adult patients with unresectable or metastatic melanoma	200 mg every 3 weeks, or 400 mg every 6 weeks	Until disease progression or unacceptable toxicity
Adjuvant treatment of adult patients with melanoma, NSCLC, or RCC	200 mg every 3 weeks, or 400 mg every 6 weeks	Until disease recurrence, unacceptable toxicity, or up to 12 months
Adult patients with NSCLC, HNSCC, cHL, PMBCL, locally advanced or metastatic urothelial carcinoma, MSI-H or dMMR cancer, MSI-H or dMMR CRC, MSI-H or dMMR endometrial carcinoma, esophageal cancer, cervical cancer, HCC, MCC, TMB-H cancer, or cSCC	200 mg every 3 weeks, or 400 mg every 6 weeks	Until disease recurrence, unacceptable toxicity, or up to 24 months
Adult patients with high-risk BCG-unresponsive NMIBC	200 mg every 3 weeks, or 400 mg every 6 weeks	Until persistent or recurrent high-risk NMIBC, disease progression, unacceptable toxicity, or up to 24 months
Pediatric patients with cHL, PMBCL, MSI-H or dMMR cancer, MCC, or TMBH cancer	2 mg/kg every 3 weeks (up to a max of 200 mg)	Until disease recurrence, unacceptable toxicity, or up to 24 months
Pediatric patients (12 years of age and older) for adjuvant treatment of melanoma	2 mg/kg every 3 weeks (up to a max of 200 mg)	Until disease recurrence, unacceptable toxicity, or up to 12 months

COMBINATION THERAPY*		
Indication	Recommended Dosage	Duration of Treatment
Adult patients with NSCLC, HNSCC, HER2-negative gastric cancer, esophageal cancer, or BTC	200 mg every 3 weeks, or 400 mg every 6 weeks. Administer prior to chemotherapy when given on the same day.	Until disease progression, unacceptable toxicity, or up to 24 months

COMBINATION THERAPY*		
Indication	Recommended Dosage	Duration of Treatment
Adult patients with resectable NSCLC	200 mg every 3 weeks, or 400 mg every 6 weeks. Administer prior to chemotherapy when given on the same day.	Neoadjuvant treatment in combination with chemotherapy for 12 weeks or until disease progression that precludes definitive surgery or unacceptable toxicity, followed by adjuvant treatment with Keytruda® as a single agent for 39 weeks or until disease recurrence or unacceptable toxicity.
Adult patients with locally advanced or metastatic urothelial carcinoma	200 mg every 3 weeks, or 400 mg every 6 weeks. Administer after enfortumab vedotin (Padcev®) when given on the same day.	Until disease progression, unacceptable toxicity, or up to 24 months
Adult patients with HER2-positive gastric cancer	200 mg every 3 weeks, or 400 mg every 6 weeks. Administer prior to trastuzumab and chemotherapy when given on the same day.	Until disease progression, unacceptable toxicity, or up to 24 months
Adult patients with cervical cancer	200 mg every 3 weeks, or 400 mg every 6 weeks Administer prior to chemotherapy with or without bevacizumab when given on the same day.	Until disease progression, unacceptable toxicity, or for Keytruda®, up to 24 months
Adult Patients with RCC	200 mg every 3 weeks, or 400 mg every 6 weeks Administer in combination with axitinib 5 mg orally twice daily** or administer in combination with lenvatinib 20 mg orally once daily.	Until disease progression, unacceptable toxicity, or for Keytruda®, up to 24 months
Adult patients with endometrial carcinoma	200 mg every 3 weeks, or 400 mg every 6 weeks Administer in combination with lenvatinib 20 mg orally once daily.	Until disease progression, unacceptable toxicity, or for Keytruda®, up to 24 months
Adult patients with high-risk early-stage TNBC	200 mg every 3 weeks, or 400 mg every 6 weeks Administer prior to chemotherapy when given on same day.	Neoadjuvant treatment in combination with chemotherapy for 24 weeks (8 doses of 200 mg every 3 weeks or 4 doses of 400 mg every 6 weeks) or until disease progression or unacceptable toxicity, followed by adjuvant treatment with Keytruda® as a single agent for up to 27 weeks (9 doses of 200 mg every 3 weeks or 5 doses of 400 mg every 6 weeks) or until disease recurrence or unacceptable toxicity***
Adult patients with locally recurrent unresectable or metastatic TNBC	200 mg every 3 weeks, or 400 mg every 6 weeks. Administer prior to chemotherapy when given on the same day.	Until disease progression, unacceptable toxicity, or up to 24 months

* Refer to the full prescribing information for the agents administered in combination with Keytruda® for recommended dosing information, as appropriate.
** When axitinib is used in combination with Keytruda®, dose escalation of axitinib above the initial 5 mg dose may be considered at intervals of 6 weeks or longer.
*** Patients who experience disease progression or unacceptable toxicity related to Keytruda® with neoadjuvant treatment in combination with chemotherapy should not receive adjuvant single agent Keytruda®.

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Keytruda prescribing information (03/2024). Merck Sharp & Dohme LLC: Rahway, NJ. Available online at www.keytrudahcp.com. Accessed May 22, 2024.

[2] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[3] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Accessed May 31, 2024. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

- Melanoma: Cutaneous (Version 2.2024 – March 3, 2024)
- Non-Small Cell Lung Cancer (Version 5.2024 – April 23, 2024)
- Head and Neck Cancers (Version 4.2024 – May 1, 2024)
- Hodgkin Lymphoma (Version 3.2024 – March 18, 2024)
- Pediatric Hodgkin Lymphoma (Version 1.2024 – May 14, 2024)
- B-Cell Lymphomas (Version 2.2024 – April 30, 2024)
- Bladder Cancer (Version 4.2024 – May 9, 2024)
- Colon Cancer (Version 3.2024 – May 24, 2024)
- Gastric Cancer (Version 2.2024 – May 29, 2024)
- Esophageal and Esophagogastric Junction Cancers (Version 3.2024 – May 6, 2024)
- Cervical Cancer (Version 3.2024 – May 6, 2024)
- Hepatocellular Carcinoma (Version 1.2024 – April 9, 2024)

- Biliary Tract Cancers (Version 2.2024 – April 19, 2024)
- Merkel Cell Carcinoma (Version 1.2024 – November 22, 2023)
- Kidney Cancer (Version 4.2024 – May 30, 2024)
- Uterine Neoplasms (Version 2.2024 – March 6, 2024)
- Squamous Cell Skin Cancer (Version 1.2024 – November 9, 2023)
- Breast Cancer (Version 2.2024 – March 11, 2024)

[4] Péus D, Newcomb N, Hofer S. Appraisal of the Karnofsky Performance Status and proposal of a simple algorithmic system for its evaluation. *BMC Med Inform Decis Mak*. 2013;13:72. Published 2013 Jul 19. doi:10.1186/1472-6947-13-72.

[5] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol.* 1982;5:649-655.

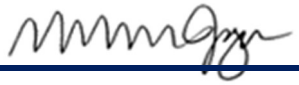
[6] Lansky SB, List MA, Lansky LL, Ritter-Sterr C, Miller DR. The measurement of performance in childhood cancer patients. Cancer. 1987 Oct 1;60(7):1651-6. PMID: 3621134.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

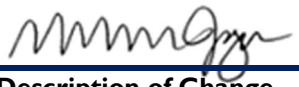
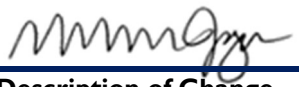
Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]			
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]			
Signature			

Change Date	Changed By	Description of Change	Version
07/19/2024	CAC	Annual review. Updated NCCN guidelines and references. Updated Appendix A with dosing for new FDA-approved indications and coding section with corresponding ICD-10 codes for new indications. Added Lansky Play Scale and Karnofsky scores to criteria of indications which are approved for use in pediatric patients (melanoma, cHL, PMBCL, MCC, MSI-H or dMMR cancer, and TMB-H cancer). 10/12/2023 (FDA): Conversion of the Merkel cell carcinoma (MCC) indication in both adult and pediatric patients from accelerated approval to regular approval. 10/16/2023: FDA approved new indication – treatment of patients with resectable (tumors ≥4 cm or node positive) NSCLC. Criteria added. 10/31/2023: FDA approved new indication – treatment of patients with locally advanced unresectable or metastatic biliary tract cancer (BTC). Criteria added. 11/07/2023: FDA label change – modification to gastric cancer indication. Added "whose tumors express PD-L1 (CPS ≥ 1)" and *patients* changed to *adults*. Updated policy to mirror indication language. 11/16/2023: FDA approved new indication – treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma. Criteria added. 12/15/2023: FDA label change – modification to urothelial carcinoma indication. Removed qualifier "who are not eligible for cisplatin-containing chemotherapy." Conversion of this indication from accelerated approval to regular approval. Criteria updated to align with label change. 01/12/2024: FDA approved new indication – treatment of patients with FIGO 2014 Stage III-IVA cervical cancer (in combination with CRT). Criteria added. 01/25/2024: FDA revised indication for HCC to read as follows: "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." Conversion of this indication from accelerated approval to regular approval. Criteria updated.	7
Signature William (Bill) Jagiello, DO			

Criteria Change History *(continued)*

Change Date	Changed By	Description of Change	Version
07/21/2023	CAC	Annual review. Moved dosing information to Appendix A. Updated NCCN references ["Guidelines for Hepatobiliary Carcinoma" separated into 2 sections, "Guidelines for Hepatocellular Carcinoma" and NCCN Guidelines for Biliary Tract Cancer). Reference HCC in policy.] 12/16/2022 (FDA): Postmarketing requirement fulfilled for alternative dosing regimen for all approved adult solid tumor indications (alternative dosing regimen for adult cHL and adult PMBCL still under accelerated approval). 8/5/2022 (FDA): Labeling updated to reflect the availability of an FDA-approved test for identifying patients with mismatch repair proficient (pMMR) advanced endometrial carcinoma. 1/26/2023 (FDA): Added criteria for new indication as a single agent, for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC. 4/3/2023 (FDA): Added criteria for new indication, in combination with Padcev®: treatment of adult patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing therapy.	6
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
04/15/2022	CAC	Annual review. Rewrite.	5
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
01/15/2021	CAC	Annual review.	4
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
04/28/2020	CAC	Changed from ETP to PA and added code J9271.	3
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
01/19/2018	CAC	Criterion #3 added "and have progression on or after platinum-based chemotherapy".	2
Signature C. David Smith, MD			
Change Date	**Changed By**	**Description of Change**	**Version**
01/15/2016	CAC	Removed dosing information. Removed reference to ipilimumab (Yervoy). Added information on non-small cell lung cancer (NSMCLC).	1
Signature			

CAC = Medicaid Clinical Advisory Committee