Geisinger

POLICIES AND PROCEDURE MANUAL

Policy: MBP 119.0

Section: Medical Benefit Pharmaceutical Policy

Subject: Keytruda (pembrolizumab)

I. Policy:
Keytruda (pembrolizumab)

II. Purpose/Objective:
To provide a policy of coverage regarding Keytruda (pembrolizumab)

III. Responsibility:
A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than
3. the department requiring/authoring the policy.
4. Devised – the date the policy was implemented.
5. Revised – the date of every revision to the policy, including typographical and grammatical changes.
6. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

Medicaid Business Segment
Medically Necessary — A service, item, procedure, or level of care compensable under the Medical Assistance program that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

i. Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
ii. Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
iii. Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.

DESCRIPTION:
Keytruda (pembrolizumab) binds to the programmed death receptor-1 (PD-1) ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells, inhibits T cell proliferation and cytokine production.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

GRANDFATHER PROVISION – Members already established on therapy are eligible for approval as long as there is medical record documentation that the safety and effectiveness of use for the prescribed indication is supported by Food and Drug Administration (FDA) approval or adequate medical and scientific evidence in the medical literature

Keytruda (pembrolizumab) will be considered medically necessary for all lines of business when all of the following criteria are met:

1. **Melanoma**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation of one of the following:

     Unresectable or metastatic melanoma:
     - Medical record documentation that patient is ≥ 18 years of age **AND**
     - A diagnosis of unresectable or metastatic melanoma **AND**
     - Keytruda is not being used in combination with any other agents for the treatment of unresectable or metastatic melanoma.

     OR

     Adjuvant treatment of completely resected melanoma
     - Medical record documentation that patient is ≥ 12 years of age **AND**
     - A diagnosis of Stage IIB, IIC, or III melanoma, which has been completely resected **AND**
     - Keytruda is being used in the adjuvant setting (following complete resection) **AND**
     - Keytruda is being used as a single agent.

2. **Neoadjuvant or Adjuvant Treatment of Non-Small Cell Lung Cancer (NSCLC)**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - Medical record documentation of one of the following:
     - Medical record documentation of Stage IB (T2a ≥ 4 cm), II, or IIIa non-small cell lung cancer (NSCLC) **AND**
     - Keytruda is being used in the adjuvant setting following resection and platinum-based chemotherapy **AND**
     - Keytruda is being used as a single agent

     OR
     - Medical record documentation of resectable (Tumors ≥ 4 cm or Node Positive) non-small cell lung cancer (NSCLC) **AND**
     - Keytruda is being used in the neoadjuvant setting in combination with platinum containing chemotherapy then continued as a single agent in the adjuvant setting following resection

3. **Metastatic Non-Small Cell Lung Cancer (NSCLC)**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - Medical record documentation of a diagnosis of metastatic NSCLC meeting <u>one</u> of the following situations:
     - Medical record documentation of stage III NSCLC, metastatic NSCLC, OR that the member is not a candidate for surgical resection or definitive chemoradiation **AND**
     - Medical record documentation that Keytruda is being used as first-line treatment **AND**
     - Medical record documentation that Keytruda is being given as monotherapy **AND**
     - Medical record documentation that tumors express PD-L1 (TPS) ≥1% as determined by an FDA-approved test AND
     - Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations

     OR
     - Medical record documentation that Keytruda is being given as monotherapy **AND**
     - Medical record documentation that tumors express PD-L1 (TPS) ≥1% as determined by an FDA-approved test **AND**
     - Medical record documentation of disease progression on or after platinum-containing chemotherapy **AND**

- For patients with EGFR or ALK genomic tumor aberrations: medical record documentation of disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.

OR

- Medical record documentation of metastatic nonsquamous NSCLC **AND**
- Medical record documentation that Keytruda will be given in combination with pemetrexed AND either carboplatin or cisplatin **AND**
- Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations

OR

- Medical record documentation that Keytruda will be given in combination with carboplatin AND either paclitaxel or nab-paclitaxel AND
- Medical record documentation that Keytruda, carboplatin, and paclitaxel (or nab-paclitaxel) are being used as first-line treatment.

4. Head and Neck Squamous Cell Carcinoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of one of the following:
  - A diagnosis of Head and Neck Squamous Cell Carcinoma that is recurrent or metastatic **AND**
  - Disease progression on or after platinum-containing chemotherapy **AND**
  - Keytruda is being used as a single agent.

OR

- A diagnosis of metastatic or unresectable, recurrent Head and Neck Squamous Cell Carcinoma **AND**
- Keytruda is being used as a first-line treatment **AND**
- Keytruda is being used as a single agent **AND**
- Tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test

OR

- A diagnosis of metastatic or unresectable, recurrent Head and Neck Squamous Cell Carcinoma **AND**
- Keytruda is being used as a first-line treatment **AND**
- Keytruda is being administered in combination with platinum chemotherapy and fluorouracil (FU)

5. Classical Hodgkin Lymphoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of Classical Hodgkin Lymphoma **AND**
- One of the following:
  a. Medical record documentation of a diagnosis of refractory Classical Hodgkin Lymphoma **OR**
  b. Medical record documentation of age greater than or equal to 18 years AND relapse following one (1) or more prior lines of therapy **OR**
  c. Medical record documentation of age less than 18 years AND relapse following two (2) or more prior lines of therapy

6. Microsatellite Instability-High Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors OR colorectal cancer
  AND
- For solid tumors:
  - Medical record documentation of progression following prior treatment(s) **AND**
  - Medical record documentation of no satisfactory alternative treatment options

7. Urothelial Carcinoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of locally advanced or metastatic urothelial carcinoma **AND**
- Medical record documentation of one of the following:
  - Disease progression during or following platinum-containing chemotherapy
    OR

- Disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
  OR
- Patient is not eligible for <u>any</u> platinum-containing chemotherapy
  OR
- Patient has high-risk, non-muscle invasive bladder cancer (NMIBC)** **AND**
- Patient's disease is unresponsive to an adequate trial of Bacillus Calmette-Guerin (BCG) therapy** **AND**
- Patient is ineligible for or has elected not to undergo cystectomy
  OR
- Keytruda is being used in combination with Padcev

**Note:

- BCG-unresponsive high-risk NMIBC is defined as persistent disease despite adequate BCG therapy, disease recurrence after an initial tumor-free state following adequate BCG therapy, or T1 disease following a single induction course of BCG.
- Adequate BCG therapy was defined as administration of at least five of six doses of an initial induction course plus either of: at least two of three doses of maintenance therapy or at least two of six doses of a second induction course.

8. Gastric Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that Keytruda will be used as first-line treatment **AND**
- Medical record documentation of one of the following:
  - Medical record documentation of a diagnosis of locally advanced unresectable or metastatic HER-2 positive gastric or gastroesophageal junction adenocarcinoma **AND**
  - Medical record documentation that tumors express PD-L1 (CPS≥1) as approved by an FDA approved test **AND**
  - Medical record documentation that Keytruda will be used in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy

  OR
  - Medical record documentation of locally advanced unresectable or metastatic HER-2 negative gastric or gastroesophageal junction (GEJ) adenocarcinoma **AND**
  - Medical record documentation that Keytruda will be used in combination with fluoropyrimidine- and platinum-containing chemotherapy

9. Cervical Cancer

- Prescription written by a hematologist/oncologist **AND**
- One of the following:
  - Medical record documentation of recurrent or metastatic cervical cancer **AND**
  - Medical record documentation that tumors express PD-L1 (CPS≥1) **AND**
  - Medical record documentation of disease progression after receiving at least one prior line of therapy

  OR
  - Medical record documentation of persistent, recurrent or metastatic cervical cancer **AND**
  - Medical record documentation that tumors express PD-L1 (CPS≥1) **AND**
  - Medical record documentation that Keytruda will be used in combination with chemotherapy (paclitaxel, cisplatin or carboplatin), with or without bevacizumab

  OR
  - Medical record documentation of FIGO 2014 Stage III-IVA cervical cancer **AND**
  - Medical record documentation that Keytruda will be used in combination with chemoradiotherapy (cisplatin and external beam radiation therapy [EBRT] followed by brachytherapy [BT])

*Note: FIGO 2014 Stage III-IVA includes patients with tumor involvement of the lower vagina with or without extension onto pelvic sidewall or hydronephrosis/non-functioning kidney or has spread to adjacent pelvic organs.

10. Primary Mediastinal Large B-cell Lymphoma (PMBCL)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of refractory primary mediastinal large B-cell lymphoma (PMBCL) **OR**
- Medical record documentation of relapse following two (2) prior lines of therapy

11. Hepatocellular Carcinoma (HCC)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of a diagnosis of hepatocellular carcinoma **AND**
- Medical record documentation of a therapeutic failure on or intolerance to sorafenib (Nexavar)

11. Merkel Cell Carcinoma (MCC)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of Merkel Cell Carcinoma **AND**
- Medical record documentation of metastatic and/or recurrent disease

12. Renal Cell Carcinoma (RCC)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of one of the following:

Advanced Renal Cell Carcinoma

- Medical record documentation of a diagnosis of advanced renal cell carcinoma **AND**
- Medical record documentation that Keytruda is being used in combination with axitinib (Inlyta) OR lenvatinib (Lenvima) **AND**
- Medical record documentation that Keytruda in combination with axitinib (Inlyta) OR lenvatinib (Lenvima) is being used as first-line treatment for advanced disease

Note: In clinical trials, advanced disease included newly diagnosed or recurrent Stage IV renal cell carcinoma.

OR

Adjuvant treatment of Renal Cell Carcinoma

- A diagnosis of renal cell carcinoma **AND**
- Documentation of intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions **AND**
- Keytruda is being used in the adjuvant setting **AND**
- Keytruda is being used as a single agent

Note: In clinical trials, intermediate-high risk category included: pT2 with Grade 4 or sarcomatoid features; pT3, any Grade without nodal involvement (N0) or distant metastases (M0); and high risk included: pT4, any Grade N0 and M0; any pT, any Grade with nodal involvement and M0. The M1 no evidence of disease (NED) category includes patients with metastatic disease who had undergone complete resection of primary and metastatic lesions.

13. Esophageal Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- One of the following:
  - Medical record documentation of a diagnosis of locally advanced or metastatic squamous cell carcinoma of the esophagus or gastroesophageal junction (GEJ) **AND**
  - Medical record documentation that tumors express PD-L1 (CPS ≥10) as determined by an FDA-approved test **AND**
  - Medical record documentation of disease progression after one or more prior lines of systemic therapy for advanced disease.
- **OR**
  - Medical record documentation of a diagnosis of locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) carcinoma not amenable to surgical resection or definitive chemoradiation **AND**
  - Medical record documentation of use in combination with platinum (oxaliplatin or cisplatin) and fluoropyrimidine-based (fluorouracil or capecitabine) chemotherapy

14. Endometrial Carcinoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of advanced endometrial carcinoma **AND**
- Medical record documentation of disease progression following at least one prior systemic therapy **AND**
- Medical record documentation that patient is not a candidate for curative surgery or radiation **AND**
- Medical record documentation of one of the following:
    - Medical record documentation that tumors are **not** microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) **AND**
    - Medical record documentation that Keytruda will be given in combination with lenvatinib (Lenvima)

  OR
    - Medical record documentation that Keytruda will be used as a single agent for treatment of tumors that are microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)

15. Tumor Mutational Burden – High (TMB-H) Solid Tumors

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of unresectable or metastatic solid tumors **AND**
- Medical record documentation that tumors are tumor mutational burden-high (TMB-H), defined as greater than or equal to 10 mutations per megabase (≥10 mut/Mb), determined by an FDA-approved test **AND**
- Medical record documentation of progression following prior treatment(s) **AND**
- Medical record documentation of no satisfactory alternative treatment options

16. Cutaneous Squamous Cell Carcinoma (cSCC)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of locally advanced, recurrent, OR metastatic cutaneous squamous cell carcinoma **AND**
- Medical record documentation that the patient's disease is not curable by surgery **AND**
- Medical record documentation that the patient's disease is not curable by radiation.

17. Triple Negative Breast Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of one of the following:
    - Medical record documentation of locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) **AND** both of the following:
        - Medical record documentation that tumors express PD-L1 [Combined Positive Score (CPS) greater than or equal to 10] as determined by an FDA approved test **AND**
        - Medical record documentation that Keytruda will be given in combination with chemotherapy (paclitaxel, paclitaxel protein-bound, or gemcitabine and carboplatin).

  OR
    - Medical record documentation of high-risk, early-stage triple-negative breast cancer (TNBC) **AND**
    - Medical record documentation that Keytruda will be given in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery

  LIMITATIONS: The treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.

18. Biliary Tract Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of locally advanced unresectable or metastatic biliary tract cancer **AND**
- Medical record documentation that Keytruda will be used in combination with gemcitabine and cisplatin

AUTHORIZATION DURATION:

For adjuvant treatment of metastatic melanoma (completely resected melanoma), neoadjuvant/adjuvant treatment of early-stage triple negative breast cancer, neoadjuvant/adjuvant treatment of non-small cell lung cancer, and adjuvant treatment of renal cell carcinoma:
Initial approval will be for 6 months. One subsequent approval will be for an additional 6 months and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

- Authorization of Keytruda for the adjuvant treatment of metastatic melanoma, of non-small cell lung cancer, and of renal cell carcinoma should not exceed the FDA-approved treatment duration of 1 year (12 months).
- Authorization of Keytruda for the treatment of early-stage triple negative breast cancer should not exceed the approved treatment duration of 24 weeks for neoadjuvant therapy and 27 weeks for adjuvant therapy.
- Authorization for the treatment of neoadjuvant/adjuvant treatment of non-small cell lung cancer should not exceed the approved treatment duration of 12 weeks of neoadjuvant treatment and 39 weeks of adjuvant therapy.

For requests exceeding the above limits, medical record documentation of the following is required:

- Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration

For all other indications:
Initial approval will be for **6 months** or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional **12 months** or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

Note: For Medicaid (GHP Family), any requests for services that do not meet criteria set in the PARP will be evaluated on a case-by-case basis.

LINE OF BUSINESS:
Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy.
REFERENCES:

1. Keytruda [prescribing information]. Whitehouse Station, NJ: Merck & Co Inc; November 2023.

This policy will be revised as necessary and reviewed no less than annually**.**

Devised: 11/18/14

Revised: 9/20/16 (new indication), 11/17/15 (NSCLC indication), 1/17/17 (NSCLC update), 5/16/17 (CHL indication), 7/18/17 (added indications, MSI-H, urothelial, updated NSCLC), 11/21/17 (gastric cancer), 7/17/18 (cervical cancer), 9/18/18 (PMBCL, urothelial, NSCLC), 1/15/19 (NSCLC, HCC, MCC), 5/21/19 (Melanoma, NSCLC, RCC), 7/16/19 (SCLC, head and neck), 9/17/19 (esophageal), 11/19/19 (endometrial), 3/17/20 (NMIBC), 7/21/20 (TMB-H and cSCC), 12/22/20 (cHL, triple neg breast), 3/16/21 (MSI-H update), 5/18/21 (esophageal update, SCLC removal), 7/6/21 (Added GEJ verbiage to PDL1+ esophageal), 7/20/21 (update gastric and cSCC), 9/21/21 (added first line RCC w/ Lenvatinib, high-risk TNBC, PDL1+ UC not eligible for cisplatin removal), 11/16/21 (cervical in combo with chemo), 1/18/22 (Adjuvant melanoma staging and age, adjuvant RCC, auth duration), 5/17/22 (add MSI-H/dMMR endometrial cancer, delete PDL1+ gastric cancer, add Medicaid PARP statement), 2/24/23 (Medicaid Business Segment, adjuvant NSCLC, LOB carve out), 6/23/23 (added UC in combo with Padcev), 7/31/23 (dMMR/MSI-H Colorectal criteria edit), 12/30/23 (references added), 1/2/24 (neoadjuvant NSCLC, Gastric, Biliary Tract edits from 12/2023), 2/23/24 (urothelial cisplatin del from Padcev, Stage III-IVA cervical cancer add)

Reviewed: 3/24/15 (removed failure on other agents)

MA UM Committee approval: 12/31/23