



CLINICAL MEDICATION POLICY	
Policy Name:	Keytruda® (Pembrolizumab)
Policy Number:	MP-014-MD-PA
Responsible Departments:	Medical Management Medical Policy; Clinical Pharmacy
Provider Notice Date:	06/01/2017
Original Effective Date:	07/01/2017
Annual Approval Date:	01/30/2018
Revision Date:	12/13/2016
Products:	Pennsylvania Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 10

Disclaimer

Gateway HealthSM (Gateway) clinical medication policy is intended to serve only as a general reference resource regarding payment and coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Gateway HealthSM may provide coverage under the medical or pharmacy benefits of the Company's Medicaid products for medically necessary intravenous infusions of Keytruda® (pembrolizumab).

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

DEFINITIONS

Medical Necessity – A service or benefit is medically necessary if it is compensable under the Medical Assistance program and if it meets any one of the following standards:

- The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition, or disability.
- The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental, or developmental effects of an illness, condition, injury, or disability.
- The service or benefit will assist the patient to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the patient and those functional capacities that are appropriate for patients of the same age.

Non-Small Cell Lung Cancer (NSCLC) – A group of lung cancers which are named by the kinds of cells found in the cancer and the appearance of those cells under a microscope. There are three main types of non-small cell lung cancer: squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. The most common form of lung cancer is non-small cell.

ALK Gene Rearrangements – Anaplastic lymphoma kinase (ALK) function oncogene is a predictive biomarker that has been identified in a subset of patients with NSCLC. The presence of the ALK arrangement is predictive of treatment benefit with ALK targeted therapies.

EGFR Mutation – Epithelial growth factor receptor (EGFR) mutation is predictive of treatment benefit from EGFR tyrosine kinase inhibitor therapy.

PD-L1 – Cytotoxic T-cell inhibition occurs when binding of the programmed death 1 (PD-1) receptor to one of its ligands, ligand 1 (PD-L1) or 2 (PD-L2). Upregulation of the PD-L1 occurs in some tumors, and it can inhibit active T-cell surveillance of tumors. Presence of the PD-L1 biomarker in tumor cells may be predictive of treatment benefit with PD-1 inhibitors.

Melanoma – A type of cancer that begins in the melanocytes. Melanoma is also referred to as malignant melanoma and cutaneous melanoma.

PROCEDURES

1. Keytruda is considered medically necessary for the following:
 - A. Keytruda is considered medically necessary as an intravenous infusion for the treatment of metastatic non-small cell lung cancer (NSCLC) when the member meets the following criteria:
 - 1) The member must be 18 years of age or older; AND
 - 2) Treatment with Keytruda is prescribed by an oncologist/hematologist; AND
 - 3) Treatment will be used in members with metastatic NSCLC whose tumors have high PD-L1 expression (Tumor Proportion Score [TPS] \geq 50%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and no prior systemic chemotherapy treatment for metastatic NSCLC; OR
 - 4) Treatment will be used in members with metastatic NSCLC whose tumors express

PD-L1 (TPS \geq 1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy; AND

a) Members with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda

5) The medication dosing is within the following prescribing-supported parameter: dose does not exceed 200 mg every three weeks

B. Keytruda is considered medically necessary for the treatment of unresectable or metastatic melanoma when the member meets the following criteria:

1) The member is 18 years of age or older; AND

2) Treatment with Keytruda is prescribed by an oncologist/hematologist; AND

3) The member has Stage III (unresectable) or IV (metastatic) disease; AND

4) The medication dosing is within the following prescribing-supported parameter: dose does not exceed 2 mg/kg every three weeks

C. Keytruda is considered medically necessary for the treatment of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) when the member meets the following criteria:

1) The member is 18 years of age or older; AND

2) Treatment with Keytruda is prescribed by an oncologist/hematologist; AND

3) The member has had progression on or after platinum-containing chemotherapy; AND

4) The medication dosing is within the following prescribing-supported parameter: dose does not exceed 200 mg every 3 weeks

2. Contraindications

Safety and effectiveness of Keytruda has not been established in pediatric members.

3. When Keytruda is not covered

Keytruda is not covered for conditions other than those listed above because the scientific evidence has not been established.

Coverage may be provided for any non-FDA labeled indication or a medically accepted indication that is supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis for which it is prescribed and will be reviewed on a case-by-case basis to determine medical necessity.

When non-formulary criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

4. Post-payment Audit Statement

The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Gateway HealthSM at any time pursuant to the terms of your provider agreement.

5. Place of Service

The place of service for the administration of Keytruda is outpatient.

Governing Bodies Approval

The FDA approved Keytruda (pembrolizumab) in September 2014 for the treatment of unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.

Keytruda was granted FDA approval in October 2015 for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors expressed programmed death ligand 1 (PD-L1) and who have disease progression on or after platinum-containing chemotherapy. The medication is also approved for patients with metastatic NSCLC epithelial growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) gene rearrangements who have disease progression on FDA-approved targeted therapy prior to receiving Keytruda. A companion laboratory test was approved to detect PD-L1 expression in non-small cell lung tumors.

CODING REQUIREMENTS

Procedure Codes:

HCPCS Code	Description
J9271	Injection, pembrolizumab, 1 mg

Diagnosis Codes:

ICD-10 Codes	Description
C00.0	Malignant neoplasm of external upper lip
C00.1	Malignant neoplasm of external lower lip
C00.2	Malignant neoplasm of external lip, unspecified
C00.3	Malignant neoplasm of upper lip, inner aspect
C00.4	Malignant neoplasm of lower lip, inner aspect
C00.5	Malignant neoplasm of lip, unspecified, inner aspect
C00.6	Malignant neoplasm of commissure of lip, unspecified
C00.8	Malignant neoplasm of overlapping sites of lip
C00.9	Malignant neoplasm of lip, unspecified
C01	Malignant neoplasm of base of tongue
C02	Malignant neoplasm of other and unspecified parts of tongue
C02.0	Malignant neoplasm of dorsal surface of tongue
C02.1	Malignant neoplasm of border of tongue
C02.2	Malignant neoplasm of ventral surface of tongue
C02.3	Malignant neoplasm of anterior two-thirds of tongue, part unspecified
C02.4	Malignant neoplasm of lingual tonsil
C02.8	Malignant neoplasm of overlapping sites of tongue
C02.9	Malignant neoplasm of tongue, unspecified
C03	Malignant neoplasm of gum
C03.0	Malignant neoplasm of upper gum
C03.1	Malignant neoplasm of lower gum
C03.9	Malignant neoplasm of gum, unspecified

C04	Malignant neoplasm of floor of mouth
C04.0	Malignant neoplasm of anterior floor of mouth
C04.1	Malignant neoplasm of lateral floor of mouth
C04.8	Malignant neoplasm of overlapping sites of floor of mouth
C04.9	Malignant neoplasm of floor of mouth, unspecified
C05	Malignant neoplasm of palate
C05.0	Malignant neoplasm of hard palate
C05.1	Malignant neoplasm of soft palate
C05.2	Malignant neoplasm of uvula
C05.8	Malignant neoplasm of overlapping sites of palate
C05.9	Malignant neoplasm of palate, unspecified
C06	Malignant neoplasm of other and unspecified parts of mouth
C06.1	Malignant neoplasm of cheek mucosa
C06.2	Malignant neoplasm of retromolar area
C06.8	Malignant neoplasm of cheek mucosa
C06.80	Malignant neoplasm of overlapping sites of unspecified parts of mouth
C06.89	Malignant neoplasm of overlapping sites of other parts of mouth
C06.9	Malignant neoplasm of mouth, unspecified
C07	Malignant neoplasm of parotid gland
C08	Malignant neoplasm of other and unspecified major salivary glands
C08.0	Malignant neoplasm of submandibular gland
C08.1	Malignant neoplasm of sublingual gland
C08.9	Malignant neoplasm of major salivary gland, unspecified
C09.0	Malignant neoplasm of tonsil
C09.1	Malignant neoplasm of tonsillar pillar (anterior)(posterior)
C09.8	Malignant neoplasm of overlapping sites of tonsil
C09.9	Malignant neoplasm of tonsil, unspecified
C10	Malignant neoplasm of oropharynx
C10.0	Malignant neoplasm of vallecular
C10.1	Malignant neoplasm of anterior surface of epiglottis
C10.2	Malignant neoplasm of lateral wall of oropharynx
C10.3	Malignant neoplasm of posterior wall of oropharynx
C10.4	Malignant neoplasm of branchial cleft
C10.8	Malignant neoplasm of overlapping sites of oropharynx
C10.9	Malignant neoplasm of oropharynx, unspecified
C11	Malignant neoplasm of nasopharynx
C11.0	Malignant neoplasm of superior wall of nasopharynx
C11.1	Malignant neoplasm of posterior wall of nasopharynx
C11.2	Malignant neoplasm of lateral wall of nasopharynx
C11.3	Malignant neoplasm of anterior wall of nasopharynx
C11.8	Malignant neoplasm of overlapping sites of nasopharynx
C11.9	Malignant neoplasm of nasopharynx, unspecified
C12	Malignant neoplasm of pyriform sinus
C13	Malignant neoplasm of hypopharynx
C13.0	Malignant neoplasm of postcricoid region
C13.1	Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect

C13.2	Malignant neoplasm of posterior wall of hypopharynx
C13.8	Malignant neoplasm of overlapping sites of hypopharynx
C13.9	Malignant neoplasm of hypopharynx, unspecified
C14	Malignant neoplasm of other ill-defined sites in the lip, oral cavity and pharynx
C14.0	Malignant neoplasm of pharynx, unspecified
C14.2	Malignant neoplasm of Waldeyer's ring
C14.8	Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx
C16	Malignant neoplasm of Stomach
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
C30	Malignant neoplasm of nasal cavity and middle ear
C30.0	Malignant neoplasm of nasal cavity
C30.1	Malignant neoplasm of middle ear
C31	Malignant neoplasm of accessory sinuses
C31.0	Malignant neoplasm of maxillary sinus
C31.1	Malignant neoplasm of ethmoidal sinus
C31.2	Malignant neoplasm of frontal sinus
C31.3	Malignant neoplasm of sphenoid sinus
C31.8	Malignant neoplasm of overlapping sites of accessory sinuses
C31.9	Malignant neoplasm of accessory sinus, unspecified
C32	Malignant neoplasm of larynx
C32.0	Malignant neoplasm of glottis
C32.1	Malignant neoplasm of supraglottis
C32.2	Malignant neoplasm of subglottis
C32.3	Malignant neoplasm of laryngeal cartilage
C32.8	Malignant neoplasm of overlapping sites of larynx
C32.9	Malignant neoplasm of larynx, unspecified
C33	Malignant neoplasm of trachea
C34	Malignant neoplasm of bronchus and lung
C34.0	Malignant neoplasm of main bronchus
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.1	Malignant neoplasm of upper lobe, bronchus or lung
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung

C34.3	Malignant neoplasm of lower lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.8	Malignant neoplasm of overlapping sites of bronchus and lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus or lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus or lung
C34.9	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.90	Malignant neoplasm of unspecified part of bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C43.	Malignant melanoma of skin
C43.0	Malignant melanoma of lip
C43.1	Malignant melanoma eyelid, including canthus
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.11	Malignant melanoma of right eyelid, including canthus
C43.12	Malignant melanoma of left eyelid, including canthus
C43.2	Malignant neoplasm of ear and external auricular canal
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.3	Malignant melanoma of other and unspecified parts of face
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.5	Malignant melanoma of trunk
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.6	Malignant melanoma of upper limb, including shoulder
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.7	Malignant melanoma of lower limb, including hip
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C44.12	Squamous cell carcinoma of skin of eyelid, including canthus
C44.121	Squamous cell carcinoma of skin of unspecified eyelid, including canthus
C44.122	Squamous cell carcinoma of skin of right eyelid, including canthus
C44.129	Squamous cell carcinoma of skin of left eyelid, including canthus

C44.22	Squamous cell carcinoma of skin of ear and external auricular canal
C44.221	Squamous cell carcinoma of skin of unspecified ear and external auricular canal
C44.222	Squamous cell carcinoma of skin of right ear and external auricular canal
C44.229	Squamous cell carcinoma of skin of left ear and external auricular canal
C44.32	Squamous cell carcinoma of skin of other and unspecified parts of face
C44.320	Squamous cell carcinoma of skin of unspecified parts of face
C44.321	Squamous cell carcinoma of skin of nose
C44.329	Squamous cell carcinoma of skin of other parts of face
C44.42	Squamous cell carcinoma of skin of scalp and neck
C69.90	Malignant neoplasm of unspecified site of unspecified eye
C69.91	Malignant neoplasm of unspecified site of right eye
C69.92	Malignant neoplasm of unspecified site of left eye
C76.0	Malignant neoplasm of head, face and neck
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C77.1	Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes
C79.31	Secondary malignant neoplasm of brain
D03	Melanoma in situ
D03.0	Melanoma in situ of lip
D03.1	Melanoma in situ of eyelid, including canthus
D03.10	Melanoma in situ of unspecified eyelid, including canthus
D03.11	Melanoma in situ of right eyelid, including canthus
D03.12	Melanoma in situ of left eyelid, including canthus
D03.2	Melanoma in situ of ear and external auricular canal
D03.20	Melanoma in situ of unspecified ear and external auricular canal
D03.21	Melanoma in situ of right ear and external auricular canal
D03.22	Melanoma in situ of left ear and external auricular canal
D03.3	Melanoma in situ of other and unspecified parts of face
D03.30	Melanoma in situ of unspecified part of face
D03.39	Melanoma in situ of other parts of face
D03.4	Melanoma in situ of scalp and neck
D03.5	Melanoma in situ of trunk
D03.51	Melanoma in situ of anal skin
D06.52	Melanoma in situ of breast (skin) (soft tissue)
D03.59	Melanoma in situ of other part of trunk
D03.6	Melanoma in situ of upper limb, including shoulder
D03.60	Melanoma in situ of unspecified upper limb, including shoulder
D03.61	Melanoma in situ of right upper limb, including shoulder
D03.62	Melanoma in situ of left upper limb, including shoulder
D03.7	Melanoma in situ of lower limb, including hip
D03.70	Melanoma in situ of unspecified lower limb, including hip
D03.71	Melanoma in situ of right lower limb, including hip
D03.72	Melanoma in situ of left lower limb, including hip
D03.8	Melanoma in situ of other sites
D03.9	Melanoma in situ, unspecified

Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.21	Personal history of malignant neoplasm of larynx
Z85.22	Personal history of malignant neoplasm of nasal cavities, middle ear, and accessory sinuses
Z85.810	Personal history of malignant neoplasm of tongue
Z85.818	Personal history of malignant neoplasm of lip, oral cavity, and pharynx
Z85.819	Personal history of malignant neoplasm of unspecified site of lip, oral cavity, and pharynx
Z85.820	Personal history of malignant melanoma of skin

REIMBURSEMENT

Participating facilities will be reimbursed per their Gateway HealthSM contract.

POLICY SOURCE(S)

Keytruda (pembrolizumab) Prescribing Information. Whitehouse Station, NJ: Merck; Dec 2015.

Pembrolizumab In: Micromedex[®] Solutions. US, Canada, UK: Truven Health Analytics Inc. Accessed on December 30, 2015.

Ettinger DS, Wood DE, Akerley W, et al. Non-small cell lung cancer. Version 4.2016. In National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines). Accessed on January 14, 2016.

Robert C, Schachter J, Long GV, et al. Pembrolizumab versus ipilimumab in advanced melanoma. N Engl J Med. 2015; 372: 2521-32. Accessed on April 27, 2016.

National Cancer Institute. What you need to know about melanoma and other skin cancers. January 11, 2011. Accessed on April 27, 2016 and available at: <http://www.cancer.gov/cancerinfo/wyntk/melanoma>.

National Comprehensive Cancer Network[®] NCCN Clinical Practice Guidelines in Oncology[™]. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>. Accessed on April 27, 2016.

- Melanoma (V.2.2016) Revised November 25, 2015
- Non-small Cell Lung Cancer (V.4.2016) Revised January 12, 2016

Policy History

Date	Activity
04/27/2016	Initial policy developed
07/01/2016	Provider effective date
12/13/2016	<p>Revisions: Annual Review, updated indications and dosage, and updated references</p> <p>Criteria changes:</p> <ul style="list-style-type: none"> • The disease/tumor criteria for NSCLC has been revised and updated - <u>OLD CRITERIA</u> <i>"The patient's disease has progressed on or after platinum-containing chemotherapy; AND If the patient has EGRF or ALK mutations, the patient has had disease progression on FDA-approved therapy (EGRF- or ALK-directed therapy) for these mutations prior to receiving Keytruda"</i> <u>NEW CRITERIA</u> <i>"Treatment will be used in members with metastatic NSCLC whose tumors have high PD-L1 expression (Tumor Proportion Score [TPS] ≥ 50%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and no prior systemic chemotherapy treatment for metastatic NSCLC; OR Treatment will be used in members 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-- Members with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda;"</i> • The ECOG criteria has been removed from the revised policy for all disease indications; • The dosing for all disease indications has been revised to follow FDA indications; • The treatment type has been updated for unresectable/metastatic melanoma - <u>OLD CRITERIA</u> <i>"The medication will be used as monotherapy for metastatic or unresectable disease as first-line therapy; OR The medication will be used as monotherapy for metastatic or unresectable disease as second-line or subsequent therapy for disease progression or following maximum clinical benefit from BRAF targeted therapy for patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 0 – "</i> <u>NEW CRITERIA</u> <i>"The member has Stage III (unresectable) or IV (metastatic) disease;"</i> • New indications were added to the revised policy for recurrent/ metastatic HNSCC <p>ALL ICD 10 codes were updated and revised. The old policy version had ranges described, it was required to have each code documented individually; codes were added to include all pertinent coding for HNSCC; C44 codes added for squamous cell carcinoma; C76 and C77 codes added for HNSCC; D03 codes added for melanoma in situ; Z codes were added for personal history.</p>
05/17/2017	QI/UM approval
07/01/2017	Provider effective date