Drug Policy:

Keytruda™ (pembrolizumab)

POLICY NUMBER UM ONC_1263	**SUBJECT** Keytruda™ (pembrolizumab)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 5**
DATES COMMITTEE REVIEWED 11/12/14, 10/14/15, 07/26/16, 08/24/16, 03/08/17, 06/14/17, 06/13/18, 05/08/19, 09/11/19, 10/09/19, 12/11/19, 02/12/20, 03/11/20, 04/08/20, 05/13/20, 06/10/20, 08/12/20	**APPROVAL DATE** August 12, 2020	**EFFECTIVE DATE** August 28, 2020	**COMMITTEE APPROVAL DATES** (latest version listed last) 11/12/14, 10/14/15, 07/26/16, 08/24/16, 03/08/17, 06/14/17, 06/13/18, 05/08/19, 09/11/19, 10/09/19, 12/11/19, 02/12/20, 03/11/20, 04/08/20, 05/13/20, 06/10/20, 08/12/20	
PRIMARY BUSINESS OWNER: UM **APPROVED BY:** Dr. Andrew Hertler		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1	**NCQA STANDARDS** UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** All	

I. PURPOSE

To define and describe the accepted indications for Keytruda (pembrolizumab) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the Preferred Drug Guidelines OR

2. When health plan Exchange coverage provisions-including any applicable PDLs (Preferred Drug Lists)-conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the Preferred Drug Guidelines OR
3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways when applicable, otherwise shall follow NCH drug policies AND
4. Continuation requests of previously approved non-preferred medication are not subject to this provision AND
5. When available, generic alternatives are preferred over brand-name drugs.

B. Melanoma

1. Keytruda (pembrolizumab) will be used as single agent for ONE of the following:
   a. Adjuvant therapy for high-risk Stage III melanoma following complete resection of the primary tumor (when identified) and a complete regional lymph node dissection. NOTE: The maximum total duration of therapy is 1 year in the adjuvant setting OR
   b. For unresectable or metastatic melanoma and the member had no prior disease progression on a PD-L1/PD-1 inhibitor.

C. Recurrent/Metastatic Squamous and Non-Squamous Non-Small Cell Lung Cancer (NSCLC)

1. NOTE #1: The preferred agent, per NCH Policy and NCH Pathway, for first line and maintenance treatment of recurrent/metastatic NSCLC is Keytruda (pembrolizumab) over other PD-1 or PD-L1 inhibitors (i.e. Opdivo, Tecentriq).
2. NOTE # 2: Keytruda (pembrolizumab) use in non-squamous/adenocarcinoma Non-Small Cell Lung Cancer, as a single agent or in combination with platinum-based chemotherapy REQUIRES that the member's NSCLC be negative for EGFR mutations, ALK rearrangements, and ROS-1 rearrangements.
3. Keytruda (pembrolizumab) will be used for ONE of the following:
   a. As first line therapy
      - As a single agent if member's NSCLC is negative for EGFR, ALK, and ROS1 (biomarkers not required for squamous histology) AND the tumor PD-L1 expression (either CPS- Combined Positive Score, or TPS- Tumor Proportion Score) is ≥ 50% OR
      - As a single agent if member's NSCLC is negative for EGFR, ALK, and ROS1 (biomarkers not required for squamous histology) AND the PDL1 is ≥ 1% and concurrent chemotherapy cannot be given or is contraindicated OR
      - In combination with pemetrexed and platinum chemotherapy in members with non-squamous histology if EGFR, ALK, and ROS1 genomic alterations are negative, regardless of the PD-L1 level OR
      - In combination with carboplatin and paclitaxel or nab-paclitaxel (if there is a history of a severe allergic reaction, anaphylaxis, or intolerance to Taxol) in members with squamous cell histology.
   b. As continuation maintenance therapy, in combination with pemetrexed (non-squamous) or as a single agent, in members who have achieved complete response/partial response/stable disease following first line therapy with a regimen that included chemotherapy + pembrolizumab.
   c. As subsequent therapy as a single agent for tumors with PD-L1 expression levels ≥ 1% and the member had no prior progression on a PD-L1/PD-1 inhibitor.

D. Head and Neck

1. The member has unresectable, recurrent, or metastatic NON-nasopharyngeal squamous cell carcinoma of the head and neck AND Keytruda (pembrolizumab) will be used for:
    a. First line therapy
        - As a single agent for tumors that express PD-L1 (either CPS- Combined Positive Score or TPS- Tumor Proportion Score) ≥ 1% OR
        - In combination with fluorouracil and platinum chemotherapy, regardless of the PD-L1 expression score.
    b. Subsequent therapy as a single agent for disease progression on or after platinum-based chemotherapy, regardless of the PD-L1 expression score.

E. Hodgkin's Lymphoma

1. The member has refractory or relapsed Hodgkin's Lymphoma and Keytruda (pembrolizumab) will be used as a single agent.

F. Urothelial Carcinoma including Upper Urinary Tract Carcinoma and Carcinoma of Urethra

1. NOTE: Per NCH Policy and NCH Pathway, Keytruda is the preferred checkpoint inhibitor rather than Opdivo, Tecentriq, Bavencio or Imfinzi, for subsequent therapy of metastatic/recurrent urothelial carcinoma.
2. The member has recurrent/metastatic urothelial cancer and Keytruda (pembrolizumab) will be used for members who are not eligible for platinum-containing chemotherapy or who have disease progression during or after platinum containing chemotherapy.

G. Colorectal Cancer

1. Therapy as a single agent for patients with metastatic colorectal cancer whose tumors show deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H]. This requires confirmation of dMMR/MSI-High status.
    a. As primary treatment for unresectable/metastatic/medically inoperable disease OR
    b. As subsequent therapy for unresectable/metastatic/medical inoperable disease.

H. Gastric Cancer of Esophageal and Esophagogastric Junction Cancers

1. The member has unresectable locally advanced, recurrent, or metastatic instability-high (MSI-H) or mismatch repair deficient OR PD-L1 positive gastric, esophageal, or esophagogastric junction cancers AND
    a. For squamous cell esophageal or esophagogastric junction cancers: Keytruda (pembrolizumab) will be used as a single agent, as second line therapy if PD-L1 is ≥ 10%, and third line therapy if PD-L1 is ≥1% OR
    b. For adenocarcinoma of the esophagus/GE junction: Keytruda will be used as third line therapy if PD-L1 is ≥1% OR
    c. For gastric cancers: Keytruda (pembrolizumab) will be used as a single agent as third line therapy if PD-L1 is ≥1%.

I. Cervical Cancer

1. The member has recurrent or metastatic microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) cervical cancer or PD-L1 positive, CPS or TPS ≥ 1%, tumors AND
2. Keytruda (pembrolizumab) will be used as a single agent as subsequent therapy following disease progression on prior chemotherapy treatment.

J. Hepatobiliary Cancers

1. Keytruda (pembrolizumab) will be used in members with hepatocellular carcinoma who have disease progression on or after sorafenib, lenvatinib, or regorafenib unless intolerance or contraindications exist to the above 3 agents OR
2. Intrahepatic/Extrahepatic Cholangiocarcinoma or Gallbladder Cancers for unresectable or metastatic disease that is microsatellite instability-high (MSI-H) and/or deficient mismatch repair (dMMR).

K. Merkel Cell Carcinoma (MCC)

1. Keytruda (pembrolizumab) will be used as a single agent in members with recurrent/locally advanced /metastatic Merkel Cell Carcinoma regardless of the line of therapy

L. Renal Cell Carcinoma (RCC)

1. NOTE: The preferred regimen for first line therapy if metastatic renal cell carcinoma- IMDC Intermediate and High Risk - is Nivolumab with or without Ipilimumab.
2. Keytruda will be used as a single agent for subsequent therapy if member has not received prior PD-1 inhibitor therapy.

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

1. Keytruda (pembrolizumab) will be used as a single agent in relapsed or refractory primary mediastinal large B-cell lymphoma.

N. Endometrial Carcinoma

1. Keytruda (pembrolizumab) will be used as a single agent as subsequent-line systemic therapy for unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumor that has progressed following prior treatment and no satisfactory alternative treatment options.
2. Keytruda will be used with Lenvatinib as subsequent therapy after disease progression on prior chemotherapy, in members whose tumors are MSI-Stable (for members with tumors that are MSI-High, single agent pembrolizumab is recommended per policy in this clinical setting- item 14.a. above).

O. Small Cell Lung Cancer (SCLC)

1. Keytruda (pembrolizumab) will be used as a single agent as subsequent therapy AND
2. The member had no prior disease progression on a PD-L1/PD-1 inhibitor.

III. EXCLUSION CRITERIA

A. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.

B. Disease progression on Keytruda (pembrolizumab) containing regimen or prior checkpoint inhibitor (PD-1/PD-L1) therapy.

C. Lack of EGFR, ALK and ROS-1 test results when being used in the first line therapy (as a single agent or in combination with chemotherapy) of metastatic/recurrent non-squamous/adenocarcinoma Non-Small Cell Lung Cancer.

D. Dosing exceeds single dose limit of Keytruda (pembrolizumab) 400 mg/m^2 every 6 weeks or 200 mg/m^2 every 3 weeks.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Keytruda prescribing information. Merck & Co. Inc. 2020.

B. Clinical Pharmacology Elsevier Gold Standard. 20120

C. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2020.

D. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2020.

E. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2020.

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