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 is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century 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.

I. INDICATIONS FOR USE/INCLUSION CRITERIA

1. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

a. 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

b. 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

c. 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: [http://pathways.newcenturyhealth.com](http://pathways.newcenturyhealth.com) AND

d. Continuation requests of previously approved non-preferred medication are not subject to this provision AND

e. When available, generic drug alternatives are preferred over Brand name drugs.

2. Melanoma

a. Keytruda (pembrolizumab) is being used as single agent for ONE of the following:

   i. Adjuvant therapy for high-risk Stage III melanoma following complete resection of the primary tumor (when identified) and a complete regional lymph node dissection (total duration of therapy is 1 year) OR
ii. For unresectable or metastatic melanoma and the member had no prior disease progression on a PD-L1/PD-1 inhibitor.

3. **Recurrent/Metastatic Squamous and Non-Squamous Non-Small Cell Lung Cancer (NSCLC)**
   a. NOTE: The preferred agent, per NCH Policies and NCH Pathways, 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).
   b. Keytruda (pembrolizumab) is being used for ONE of the following:
      i. As first line therapy:
         a. As a single agent if EGFR, ALK, or ROS1 negative or both tissue biopsy and liquid biopsy are unsuccessful in providing sufficient diagnostic material AND PD-L1 expression (either CPS- Combined Positive Score, or TPS- Tumor Proportion Score) is \( \geq 50\% \) OR
         b. As a single agent in cases where the PDL1 is \( \geq 1\% \) and concurrent chemotherapy cannot be given or is contraindicated OR
         c. In combination with pemetrexed and platinum chemotherapy in members with non-squamous histology if EGFR, ALK, or ROS1 genomic alterations are negative or unknown, regardless of the PD-L1 level OR
         d. In combination with carboplatin and paclitaxel or nab-paclitaxel (if there is a history of anaphylaxis or intolerance to paclitaxel or if paclitaxel is contraindicated) in members with squamous cell histology.
      ii. As continuation maintenance therapy, in combination with pemetrexed 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].
      iii. As subsequent therapy as a single agent for tumors with PD-L1 expression levels \( \geq 1\% \) and the member had no prior progression on a PD-L1/PD-1 inhibitor.

4. **Head and Neck**
   a. The member has unresectable, recurrent, or metastatic NON-nasopharyngeal squamous cell carcinoma of the head and neck AND Keytruda (pembrolizumab) is being used as the following:
      i. First line therapy
         1. As a single agent for tumors express PD-L1 (either CPS- Combined Positive Score or TPS- Tumor Proportion Score) \( \geq 1\% \) OR
         2. In combination with fluorouracil and platinum based chemotherapy, for tumors with PD-L1 expression (either CPS- Combined Positive Score or TPS- Tumor Proportion Score) \( \geq 1\% \) OR
         3. In combination with fluorouracil and platinum chemotherapy, regardless of the PD-L1 expression score.
      ii. Subsequent therapy as a single agent for disease progression on or after platinum based chemotherapy.

5. **Hodgkin’s Lymphoma**
   a. The member has refractory or relapsed Hodgkin’s Lymphoma and Keytruda (pembrolizumab) is being used as a single agent.
6. **Urothelial Carcinoma**
   a. **NOTE:** Per NCH Policies and NCH Pathways, Keytruda is the preferred checkpoint inhibitor rather than Opdivo, Tecentriq, Bavencio or Imfinzi, for subsequent therapy of metastatic/recurrent urothelial carcinoma.
   b. The member has recurrent/metastatic urothelial cancer and Keytruda (pembrolizumab) is being used for members who are not eligible for platinum-containing chemotherapy or who have disease progression during or after platinum containing chemotherapy.

7. **Colorectal Cancer**
   a. 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 or MSI-High test results.
      i. As primary treatment for unresectable/metastatic/medically inoperable disease OR
      ii. As subsequent therapy for unresectable/metastatic/medical inoperable disease.

8. **Gastric Cancer or Esophageal and Esophagogastric Junction Cancers**
   a. The member has unresectable locally advanced, recurrent, or metastatic instability-high (MSI-H)/mismatch repair deficient OR PD-L1 positive gastric, esophageal, or esophagogastric junction cancers AND
   b. Keytruda (pembrolizumab) is being used as a single agent, as second line therapy if PD-L1 is ≥1% and third line therapy regardless of PD-L1 status.

9. **Cervical Cancer**
   a. 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
   b. Keytruda (pembrolizumab) is being used as a single agent as subsequent therapy following disease progression on prior chemotherapy treatment.

10. **Hepatobiliary Cancers**
    a. Keytruda (pembrolizumab) is being 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
    b. Intrahepatic/Extrahepatic Cholangiocarcinoma or Gallbladder Cancers for unresectable or metastatic disease that is microsatellite instability-high (MSI-H) and/or deficient mismatch repair (dMMR).

11. **Merkel Cell Carcinoma (MCC)**
    a. Keytruda (pembrolizumab) is being used as a single agent in members with recurrent/locally advanced /metastatic Merkel Cell Carcinoma

12. **Renal Cell Carcinoma (RCC)**
    a. Keytruda (pembrolizumab) is being used in combination with axitinib for members with advanced RCC and no prior disease progression on a PD-L1/PD-1 inhibitor OR
    b. Keytruda is being used as a single agent for initial or subsequent therapy.
13. **Primary Mediastinal Large B-Cell Lymphoma (PMBCL)**
   a. Keytruda (pembrolizumab) is being used as a single agent in relapsed or refractory primary mediastinal large B-cell lymphoma.

14. **Endometrial Carcinoma**
   a. Keytruda (pembrolizumab) is being 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.
   b. Keytruda is being used with Lenvatinib as subsequent therapy after disease progression on prior chemotherapy.

15. **Small Cell Lung Cancer (SCLC)**
   a. Keytruda (pembrolizumab) is being used as a single agent as subsequent therapy **AND**
   b. The member had no prior disease progression on a PD-L1/PD-1 inhibitor.

II. **EXCLUSION CRITERIA**
   1. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.
   2. Disease progression on prior checkpoint inhibitor (PD-1/PD-L1) therapy.

III. **MEDICATION MANAGEMENT**
    Please refer to the FDA label/package insert for details regarding these topics.

IV. **APPROVAL AUTHORITY**
   1. Review – Utilization Management Department
   2. Final Approval – Utilization Management Committee

V. **ATTACHMENTS**
   None

VII. **REFERENCES**