Keytruda (pembrolizumab)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Keytruda (pembrolizumab)

APPROVAL CRITERIA

Requests of Keytruda (pembrolizumab) may be approved if the following criteria are met:

I. Individual has a diagnosis of locoregional unresectable or metastatic Adrenocortical Carcinoma (NCCN 2A); **AND**
   A. Individual is using as single agent, or in combination with mitotane; **AND**
   B. Individual has a current ECOG performance status of 0-2; **AND**
   C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

II. Individual has a diagnosis of locally advanced unresectable or metastatic Biliary Tract Cancer (BTC) (Label, NCCN 1, 2A); **AND**
   A. Individual is using in combination with cisplatin and gemcitabine; **AND**
   B. Individual has not received prior systemic therapy in the advanced or metastatic setting; **AND**
   C. Individual has a current ECOG performance status of 0-2; **AND**
   D. Individual has not received treatment with another anti-PD-1, anti-PD-L1, anti-PD-L2 agent, or with an agent directed to another stimulatory or coinhibitory T-cell receptor (e.g., CTLA-4 agent); **AND**
   E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

III. Individual has a diagnosis of locally recurrent, unresectable, or metastatic Triple-Negative Breast Cancer (TNBC) (Label, NCCN 1, 2A); **AND**
   A. Individual is using in combination with paclitaxel/nab-paclitaxel, or in combination with gemcitabine and a platinum agent); **AND**
   B. Individual has a tumor with PD-L1 gene expression with Combined Positive Score (CPS) of greater than or equal to 10; **AND**
   C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**

D. Individual has a current Eastern Cooperative Group (ECOG) performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

IV. Individual has a diagnosis of high risk early-stage Triple-Negative Breast Cancer (TNBC) (Label, NCCN 2A); **AND**
A. Individual is using in combination with chemotherapy in the neoadjuvant setting; **AND**
B. Individual will continue/is continuing Keytruda as single agent in the adjuvant setting after surgical intervention; **AND**
C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
D. Individual has a current Eastern Cooperative Group (ECOG) performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

V. Individual has a diagnosis of persistent, recurrent or metastatic Cervical Cancer (Label, NCCN 1); **AND**
A. Individual is using in combination with paclitaxel and a platinum agent, with or without bevacizumab; **AND**
B. Individual has a tumor with PD-L1 gene expression with Combined Positive Score (CPS) of greater than or equal to 1 (CPS ≥ 1); **AND**
C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
D. Individual has a current Eastern Cooperative Group (ECOG) performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

VI. Individual has a diagnosis of recurrent or metastatic Cervical Cancer; **AND**
A. Individual is using as monotherapy; **AND**
B. Individual has a tumor with PD-L1 gene expression with Combined Positive Score (CPS) of greater than or equal to 1; **AND**
C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1agent; **AND**
D. Individual has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

VII. Individual has a diagnosis of FIGO 2014 Stage III-IVA cervical cancer (Label, NCCN 2A); **AND**
   A. Individual is using in combination with chemoradiotherapy (Cisplatin or carboplatin (if cisplatin intolerant) plus external beam radiation therapy [EBRT] followed by brachytherapy (CRT)); **AND**
   B. No prior definitive surgery, radiation, or systemic therapy for cervical cancer; **AND**
   C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

VIII. Individual has a diagnosis of metastatic Anal Cancer (NCCN 2A): **AND**
   A. Individual is using as second-line or subsequent therapy; **AND**
   B. Individual is using as monotherapy; **AND**
   C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

IX. Individual has a diagnosis of Colorectal Cancer (Label, NCCN 2A); **AND**
   A. Individual is using as monotherapy; **AND**
   B. Individual meets **one** of the following criteria:
      1. Primary treatment as a single agent for unresectable metachronous metastases (deficient mismatch repair/high microsatellite instability [dMMR/MSIH] only) and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months; **OR**
      2. Subsequent therapy as a single agent (if nivolumab or pembrolizumab not previously given) for unresectable, locally advanced, or metastatic disease (dMMR/MSIH only) following previous treatment with the following:
         a. Oxaliplatin-, irinotecan-, and/or fluoropyrimidine-based therapy; **OR**
         b. First line treatment as a single agent for unresectable, advanced, or metastatic disease (dMMR/MSIH only);

   AND

   C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   D. Individual has a current ECOG performance status of 0-2; **AND**
   E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

X. Individual has a diagnosis of locally advanced, regional, recurrent, or metastatic Cutaneous Squamous Cell Carcinoma (cSCC) (Label, NCCN 2A); **AND**
   A. Individual is using as monotherapy; **AND**
   B. Disease is not curable by surgery or radiation; **AND**
   C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   D. Individual has a current ECOG performance status of 0-2; **AND**
   E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XI. Individual has a diagnosis of advanced Endometrial cancer (Stage III-IV) (NCCN 1); **AND**
   A. One of the following:
      1. Using in combination with carboplatin and paclitaxel; **OR**
      2. Using as a single agent for maintenance therapy;

OR

XII. Individual has a diagnosis of advanced Endometrial Cancer (Label, NCCN 1, 2A); **AND**
   A. Individual is using in one of the following ways:
      1. Individual is using in combination with lenvatinib; **AND**
      2. Individual is mismatch repair proficient (PMMR) or not microsatellite instability high (MSI-H); **AND**
      3. One of the following:
         a. Individual has disease progression after one or more prior lines of systemic therapy; **OR**
         b. Individual has recurrent disease after prior platinum-based therapy in any setting, including neoadjuvant and adjuvant therapy;

      OR

      4. Individual is using as a single agent; **AND**
      5. Individual is MSI-H or dMMR; **AND**
      6. Individual is not a candidate for curative surgery or radiation; **AND**
      7. Individual has disease progression after one or more prior lines of systemic therapy;

   AND

   B. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   C. Individual has a current ECOG performance status of 0-2; **AND**
   D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XIII. Individual has a diagnosis of recurrent locally advanced or metastatic squamous cell Esophageal Cancer (Label, NCCN 1); **AND**
   A. Individual is using as monotherapy; **AND**
   B. Individual has a tumor with PD-L1 gene expression with CPS of greater than or equal to 10; **AND**
   C. Individual has demonstrated disease progression after one or more prior lines of systemic therapy; **AND**
   D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   E. Individual has a current ECOG performance status of 0-2; **AND**
   F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XIV. Individual has a diagnosis of unresectable, recurrent locally advanced, or metastatic Esophageal Cancer (Label, NCCN 1, 2A); **AND**
   A. Individual is using in combination with platinum and fluoropyrimidine-based chemotherapy; **AND**
   B. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   C. Individual has a current ECOG performance status of 0-2; **AND**
   D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XV. Individual has a diagnosis of locally advanced unresectable, recurrent, or metastatic Esophageal or Esophagogastric Junction cancer (NCCN 1); **AND**
   A. Individual has HER2-positive disease and is using as first line treatment; **AND**
   B. Individual is using in combination with trastuzumab or its biosimilar, platinum- and fluoropyrimidine-based chemotherapy; **AND**
   C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   D. Individual has a current ECOG performance status of 0-2; **AND**
   E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XVI. Individual has a diagnosis of unresectable locally advanced, recurrent, or metastatic Esophageal or Esophagogastric Junction cancer (NCCN); **AND**
   A. Individual has one of the following:
      1. MSI-H or dMMR tumor (independent of PD-L1 status) (NCCN 2A); **OR**
      2. HER2 overexpression negative adenocarcinoma and PD-L1 CPS ≥ 10 for palliative therapy (NCCN 1); **OR**
      3. Squamous cell carcinoma for palliative therapy (NCCN 1, 2A);

AND

B. Individual is using in combination with platinum- and a fluoropyrimidine-based chemotherapy; **AND**
C. Individual has a current ECOG performance status of 0-2; **AND**
D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XVII. Individual has a diagnosis of recurrent locally advanced unresectable, or metastatic Gastric or Gastroesophageal Junction Adenocarcinoma (Label, NCCN 2A); **AND**
A. Individual is using as monotherapy; **AND**
B. Individual has a tumor with PD-L1 gene expression with CPS of greater than or equal to 1; **AND**
C. Individual has demonstrated disease progression on or after two or more prior lines of therapy including fluoropyrimidine and platinum-containing chemotherapy, if appropriate HER2/neu-targeted therapy; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual has a current ECOG performance status of 0-2; **AND**
F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XVIII. Individual has a diagnosis of locally advanced unresectable or metastatic Gastric or Gastroesophageal Junction Adenocarcinoma (Label, NCCN 1); **AND**
A. Individual is using in one of the following ways:
1. MSI-H or dMMR tumor (independent of PD-L1 status) (NCCN 2A); **OR**
2. Individual has HER2-positive disease and is using as first line treatment; **OR**
3. Individual has HER2-negative disease and is using as first line treatment and PD-L1 CPS ≥ 10;

AND

B. Individual is using in combination with trastuzumab or its biosimilar, platinum- and fluoropyrimidine-based chemotherapy; **AND**
C. Individual has a current ECOG performance status of 0-2; **AND**
D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XIX. Individual has a diagnosis of metastatic or locally advanced Gastric cancer; **AND**
A. Individual has one of the following:
1. Individual has MSI-H or dMMR tumor (independent of PD-L1 status (NCCN 2A); **AND**
2. Individual is using as a single agent or as systemic therapy in combination with platinum- and a fluoropyrimidine-based chemotherapy;

OR

3. Individual has HER2 overexpression negative adenocarcinoma and PD-L1 CPS ≥ 1 (NCCN 1); **AND**
4. Individual is using as systemic therapy in combination with platinum- and a fluoropyrimidine-based chemotherapy;

AND

B. Individual has a current ECOG performance status of 0-2; **AND**
C. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XX. Individual has a diagnosis of relapsed or refractory primary cutaneous anaplastic large cell lymphoma (ALCL); **AND**
   A. Individual has multifocal lesions with ALCL or cutaneous ALCL with regional node; **AND**
   B. Individual is using as monotherapy; **AND**
   C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXI. Individual has a diagnosis of malignant chemotherapy-resistant gestational trophoblastic neoplasia; **AND**
   A. Individual has one of the following:
      1. High-risk disease; **OR**
      2. Recurrent or progressive intermediate trophoblastic tumor following treatment with a platinum-based regimen;

   AND

   B. Individual is using as monotherapy; **AND**
   C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXII. Individual has a diagnosis of recurrent, unresectable, or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) (Label, NCCN 1, 2A); **AND**
   A. Individual is using as monotherapy; **AND**
   B. Individual meets one of the following:
      1. Individual is using as first-line treatment for tumor with PD-L1 gene expression with CPS of greater than or equal to 1; **OR**
      2. Individual has demonstrated disease progression on or after platinum-containing chemotherapy;

OR

C. Individual is using in combination; **AND**
D. Individual meets one of the following:
    1. Individual is using as first-line treatment in combination with platinum-containing chemotherapy and fluorouracil regardless of PD-L1 expression (NCCN 2A); **OR**
        a. Individual is using as first or subsequent-line in combination with platinum-containing chemotherapy and docetaxel; **AND**
E. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
F. Individual has a current ECOG performance status of 0-2; **AND**
G. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXIII. Individual has a diagnosis of recurrent, unresectable, or metastatic cancer of the nasopharynx (NCCN 2A); **AND**
A. Individual has squamous cell carcinoma with mixed subtypes; **AND**
B. Individual is using as first-line systemic therapy or subsequent-line (if not previously used); **AND**
C. Individual is using in combination with cisplatin and gemcitabine; **AND**
D. Individual is determined to not be amenable to definitive surgery or radiation therapy; **AND**
E. Individual has a current ECOG performance status of 0-2; **AND**
F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXIV. Individual has a diagnosis of Hepatocellular Carcinoma (HCC) (Label, NCCN 2A); **AND**
A. Individual has Child-Pugh Class A advanced HCC; **AND**
B. Individual is using as monotherapy; **AND**
C. Individual has demonstrated disease progression or intolerance on or after treatment with an approved first-line agent; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual has a current ECOG performance status of 0-2; **AND**
F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXV. Individual has a diagnosis of relapsed or refractory Hodgkin lymphoma, except for those with lymphocyte-predominant Hodgkin lymphoma (Label, NCCN 2A);

OR

XXVI. Individual has a diagnosis of Kaposi Sarcoma (NCCN 2A); **AND**

A. Individual has endemic or classic Sarcoma; **AND**
B. Individual is using as subsequent therapy for relapsed/refractory advanced cutaneous, oral, visceral, or nodal disease that has progressed on or not responded to previous first-line systemic therapies; **AND**
C. Individual is using as monotherapy;
D. Individual has current ECOG performance status of 0-2; **AND**
E. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXVII. Individual has a diagnosis of Melanoma (cutaneous and uveal) (Label, NCCN 2A); **AND**
A. Individual has unresectable or metastatic melanoma; **AND**
B. Individual is using as monotherapy; **AND**
C. Individual meets one of the following:
1. Individual is using as first-line therapy in untreated disease; **AND**
2. Individual has current ECOG performance status of 0-2; **AND**
3. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
4. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

5. Individual is using as second-line or subsequent therapy for disease progression while receiving or since completed most recent therapy and/or intolerance to previous therapy; **AND**
6. Individual has a current ECOG performance status of 0-2;

OR

XXVIII. Individual has a diagnosis of Melanoma (cutaneous) (Label, NCCN 1, 2A); **AND**
A. Individual has resected, stage IIB, IIC or high-risk stage III disease; **AND**
B. Individual is using as monotherapy; **AND**
C. Individual is using adjuvant therapy for up to 12 months; **AND**
D. Individual has current ECOG performance status of 0-2; **AND**
E. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXIX. Individual has a diagnosis of Melanoma (cutaneous) (NCCN 2A); **AND**
A. Individual Is using Keytruda (pembrolizumab) in combination with low-dose Yervoy (ipilimumab) for a total of four doses, followed by pembrolizumab every 3 weeks as monotherapy for 2 years; **AND**

B. The combination is used as second-line or subsequent therapy for progression following anti-PD-1 therapy in advanced melanoma; **AND**
C. Individual has not previously used a combination of Yervoy (ipilimumab) and anti-PD-1; **AND**
D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXX. Individual has a diagnosis of metastatic or unresectable Melanoma (cutaneous) (NCCN 2A); **AND**
A. Individual is BRAF V600E mutation positive; **AND**
B. Individual is using in combination with trametinib and dabrafenib; **AND**
C. Individual is using as second-line or subsequent therapy following disease progression or intolerance if BRAF/MEK and/or PD(L)-1 inhibitor was not previously used;

OR

XXXI. Individual has a diagnosis of metastatic Melanoma with brain metastases (NCCN 2A); **AND**
A. Individual has a primary diagnosis of BRAF non-specific melanoma; **AND**
B. Individual is using as single agent for brain metastases; **AND**
C. Individual has a current ECOG performance status of 0-2; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXXII. Individual has a diagnosis of Merkel Cell Carcinoma (MCC) (Label, NCCN 2A); **AND**
A. Individual is using as monotherapy; **AND**
B. Individual has presence of metastatic or advanced locoregional MCC determined to be not amenable to definitive surgery or radiation therapy; **AND**
C. Individual has a current ECOG performance status of 0-2; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXXIII. Individual has a diagnosis of Adrenal Gland Tumor (NCCN 2A); **AND**
A. Individual has locoregional unresectable or metastatic adrenocortical carcinoma; **AND**
B. Individual is using in combination with or without mitotane; **AND**
C. Individual has a current ECOG performance status of 0-2; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**

E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXXIV. Individual has a diagnosis of Malignant Pleural Mesothelioma (Label); **AND**
- A. Individual has an unresectable advanced or metastatic disease; **AND**
- B. Individual is using in combination with pemetrexed and platinum chemotherapy; **AND**
- C. Individual is using as first-line treatment; **AND**
- D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant; **AND**
- F. Individual has a current ECOG performance status of 0-2;

OR

XXXV. Individual has a diagnosis of Primary Mediastinal Large B-Cell Lymphoma (Label, NCCN 2A); **AND**
- A. Individual is using in one of the following ways:
  1. Individual is using as monotherapy; **AND**
  2. Individual is using to treat refractory disease or subsequent therapy for disease relapse after receiving two or more prior lines of therapy;

  OR
  3. Individual is 18 years and younger using in combination with brentuximab vedotin after a partial response to second-line therapy (Pediatric Aggressive Mature B-Cell Lymphomas NCCN Guideline); **AND**
- B. Individual has a current ECOG performance status 0-2; **AND**
- C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXXVI. Individual has a diagnosis of resectable Stage II, IIIA, or IIIB (N2) Non-Small Cell Lung Cancer (NSCLC) (Label, NCCN 1, 2A); **AND**
- A. Individual is using in one of the following ways:
  1. Individual is using in combination with platinum-containing chemotherapy as neoadjuvant therapy; **OR**
  2. individual is using as a single agent for post-surgical adjuvant treatment for resectable (tumors≥ 4 cm or node positive) NSCLC;

AND
- B. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXXVII. Individual has a diagnosis of Stage IB (T2a ≥ 4cm), II, or IIIA Non-Small Cell Lung Cancer (NSCLC) (Label, NCCN 1, 2A); **AND**
- A. Individual is using as adjuvant treatment; **AND**
- B. Individual is using following resection and prior platinum-based chemotherapy; **AND**
- C. Individual is using as monotherapy; **AND**
- D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- E. Individual has a current ECOG performance status of 0-2; **AND**
- F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXXVIII. Individual has a diagnosis of advanced, recurrent, or metastatic Non-Small Cell Lung Cancer (NSCLC) (Label, NCCN 1, 2A); **AND**
- A. Individual is using for the first-line treatment; **AND**
- B. Individual's disease is stage III or IV NSCLC; **AND**
- C. Individual is using as monotherapy; **AND**
- D. Tumor expresses PD-L1 gene on at least 1% or greater of tumor cells; **AND**
- E. Individual does not have presence of actionable molecular markers*; **AND**
- F. Individual has not received another anti-PD-1 or anti-PD-L1 agent and has not undergone previous systemic therapy for metastatic disease; **AND**
- G. Individual has a current ECOG performance status of 0-2; **AND**
- H. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XXXIX. Individual has a diagnosis of advanced, recurrent, or metastatic nonsquamous NSCLC (Label, NCCN 1, 2A); **AND**
- A. Individual is using for first-line treatment; **AND**
- B. Disease is stage IIIb or IV NSCLC; **AND**
- C. Individual is using in combination with pemetrexed and a platinum agent; **AND**
- D. Individual does not have presence of actionable molecular markers*; **AND**
- E. Individual has not received another anti-PD-1 or anti-PD-L1 agent and has not undergone previous systemic therapy for metastatic disease; **AND**
- F. Individual has a current ECOG performance status of 0-2; **AND**
- G. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XL. Individual has a diagnosis of advanced, recurrent or metastatic squamous NSCLC (Label, NCCN 1, 2A); **AND**
- A. Individual is using for first line treatment; **AND**
- B. Disease is stage IV NSCLC; **AND**

C. Individual is using combination with carboplatin plus paclitaxel or nab-paclitaxel; **AND**
D. Individual does not have presence of actionable molecular markers*; **AND**
E. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent and has not undergone previous systemic therapy for metastatic disease; **AND**
F. Individual has a current ECOG performance status of 0-2; **AND**
G. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XLI. Individual has a diagnosis of advanced, recurrent, or metastatic nonsquamous NSCLC (NCCN 1, 2A); **AND**
A. Individual is using in combination with pemetrexed as **continuation maintenance therapy**, if given first-line as part of pembrolizumab/pemetrexed and platinum-based regimen; **AND**
B. Individual has tumor response or stable disease following initial cytotoxic therapy; **AND**
C. Individual has not received another anti-PD-1 or anti-PD-L1 agent; **AND**
D. Individual has a current ECOG performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XLII. Individual has a diagnosis of advanced, recurrent, or metastatic squamous cell NSCLC (NCCN 2A); **AND**
A. Individual is using as monotherapy as **continuation maintenance therapy**, if given first-line as part of pembrolizumab/carboplatin/paclitaxel (or nab-paclitaxel) regimen; **AND**
B. Individual has tumor response or stable disease following initial cytotoxic therapy; **AND**
C. Individual has not received another anti-PD-1 or anti-PD-L1 agent; **AND**
D. Individual has a current ECOG performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XLIII. Individual has a diagnosis of advanced, recurrent, or metastatic NSCLC (NCCN 1, 2A); **AND**
A. Individual is using as monotherapy in second or subsequent line of therapy; **AND**
B. Individual has tumor with PD-L1 gene expression level greater than or equal to 1% with disease progression on or after platinum-containing chemotherapy;
AND
C. If individual has anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) genomic tumor aberrations are present, must have disease progression on U.S. Food and Drug Administration (FDA) approved therapy for

the aberrations prior to receiving pembrolizumab (Keytruda);
AND

D. Individual has a current ECOG performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a- systemic immunosuppressant;

OR

XLIV. Individual has a diagnosis of metastatic NSCLC with brain metastases (NCCN 2A); **AND**

A. Individual has a primary diagnosis of non-small cell lung cancer; **AND**
B. Individual is using as single agent for brain metastases; **AND**
C. Individual has tumor with PD-L1 gene expression level greater than or equal to 1%; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual has a current ECOG performance status of 0-2; **AND**
F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XLV. Individual has diagnosis of recurrent or refractory hypermutant tumor pediatric diffuse high-grade glioma (NCCN 2A); **AND**

A. Individual is using as a single agent; **AND**
B. Individual has not received treatment with another PD-1 or anti-PD-L1 agent; **AND**
C. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XLVI. Individual has diagnosis of relapsed or refractory Mycosis fungoides/Sezary syndrome (NCCN 2A); **AND**

A. Individual is using for one of the following:
    1. Individual is using as primary treatment for systemic therapy in stage III Mycosis fungoides (MF) or Stage IV Sezary Syndrome; **OR**
    2. Individual is using as subsequent therapy for refractory disease to multiple previous therapies for Stage IIB MF with limited tumor or generalized tumor lesions, Stage III MF, Stage IV Sezary Syndrome, Stage IVA2 non-Sezary or stage IVB visceral disease;

AND

B. Individual has not received treatment with another PD-1 or anti-PD-L1 agent; **AND**
C. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XLVII. Individual has diagnosis of advanced Renal Cell Carcinoma (RCC) (Label, NCCN 1); **AND**

A. Using in one of the following ways:

1. Individual is using as first-line therapy; **AND**
2. Individual is using in combination with axitinib *or* lenvatinib; **AND**
3. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
4. Individual has a current Karnofsky performance status of ≥ 70%; **AND**
5. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

6. Individual is using as subsequent therapy; **AND**
7. Individual is using in combination with axitinib or lenvatinib; **AND**
8. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XLVIII. Individual has diagnosis of Renal Cell Carcinoma (RCC) (Label, NCCN 2A); **AND**

A. Individual is using as adjuvant treatment in those with intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions; **AND**
B. Individual has not received treatment with another PD-1 or anti-PD-L1 agent; **AND**
C. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XLIX. Individual has a diagnosis of Renal Cell Carcinoma (RCC) (NCCN 2A); **AND**

A. Individual has RCC with non-clear cell histology; **AND**
B. Individual is using as single-agent therapy for relapse or stage IV disease as systemic therapy; **AND**
C. Individual has not received treatment with another PD-1 or anti-PD-L1 agent; **AND**
D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

L. Individual has a diagnosis of Ovarian cancer (NCCN 2A); **AND**

A. Individual is using for platinum-resistant persistent disease; **OR**
B. Individual is using for recurrence in combination with oral cyclophosphamide and bevacizumab (or its biosimilars); **AND**
C. Individual has not received treatment with another PD-1 or anti-PD-L1 agent; **AND**
D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LI. Individual has a diagnosis of alveolar soft part sarcoma (ASPS) (NCCN 2A); **AND**
- A. Individual is using in combination with axitinib (Inlyta); **AND**
- B. Individual has not received treatment with another anti PD-1 or anti PD-L1 agent; **AND**
- C. Individual has a current ECOG performance status of 0-1; **AND**
- D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LII. Individual has a diagnosis of unresectable, recurrent, advanced, or metastatic Soft Tissue Sarcoma (NCCN 2A); **AND**
- A. Individual is using as monotherapy for first line or subsequent therapy; **AND**
- B. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- C. Individual has a current ECOG performance status of 0-2; **AND**
- D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LIII. Individual has a diagnosis of unresectable or metastatic solid tumors (Label, NCCN 2A); **AND**
- A. Individual is using as monotherapy; **AND**
- B. One of the following:
  1. Individual has high tumor mutation burden (TMB) (greater than or equal to 10 mutations per megabase); **OR**
  2. Individual has a dMMR/MSI-H tumor; **AND**
- C. Individual has disease progression following prior treatment with no other satisfactory alternative treatment options; **AND**
- D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- E. Individual has a current ECOG performance status of 0-2; **AND**
- F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LIV. Individual has a diagnosis of relapsed or refractory primary cutaneous anaplastic large cell lymphoma (ALCL) (NCCN 2A); **AND**
- A. Disease is either ALCL with multifocal lesions or cutaneous ALCL (excluding systemic ALCL); **AND**
- B. Individual is using as a single agent; **AND**
- C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- D. Individual has a current ECOG performance status of 0-2; **AND**
- E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LV. Individual has a diagnosis of relapsed or refractory extranodal NK-T-cell lymphoma; **AND**

A. Individual is using following treatment with asparaginase-based regimen; **AND**
B. Individual is using as monotherapy; **AND**
C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
D. Individual has a current ECOG performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LVI. Individual has a diagnosis of unresectable or metastatic Thymic Carcinoma (NCCN 2A); **AND**

A. Individual is using as monotherapy; **AND**
B. Individual has disease progression following chemotherapy, or intolerance to first-line combination regimens; **AND**
C. Individual does not have thymomas; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual has a current ECOG performance status of 0-2; **AND**
F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LVII. Individual has a diagnosis of metastatic anaplastic thyroid disease (NCCN 2A); **AND**

A. Individual is using in combination with lenvatinib; **AND**
B. Individual is using as first-line or second-line therapy; **AND**
C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
D. Individual has a current ECOG performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LVIII. Individual has a diagnosis of locally advanced or metastatic Urothelial Carcinoma (Label, NCCN 2A); **AND**

A. Individual is using in combination with enfortumab vedotin (Padcev); **AND**
B. Individual is not eligible for cisplatin-containing chemotherapy; **AND**
C. Individual has a current ECOG performance status of 0-2; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LIX. Individual has a diagnosis of locally advanced or metastatic Urothelial Carcinoma (Label, NCCN 1, 2A); **AND**

A. Individual is using as monotherapy; **AND**

B. Individual meets one of the following:

1. Individual is not eligible for any platinum-containing chemotherapy; **OR**
2. Individual is using as subsequent therapy; **OR**
3. Individual has disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy;

AND

C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**

D. Individual has a current ECOG performance status of 0-2; **AND**

E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LX. Individual has a diagnosis of high-risk non-muscle invasive (T1, high grade Ta, and/or carcinoma in situ [CIS]) Urothelial Carcinoma of the Bladder with or without papillary tumors (Label, NCT02625961, NCCN 2A); **AND**

A. Individual has Bacillus Calmette-Guerin (BCG)- unresponsive disease defined as one of the following:

1. Persistent disease despite adequate BCG therapy (adequate defined as administration of at least 5 doses of an initial induction course *plus either* at least 2 doses of maintenance therapy or at least 2 doses of a second induction course); **OR**
2. Disease recurrence after an initial tumor-free state following adequate BCG therapy (adequate defined as administration of at least 5 doses of an initial induction course *plus either* at least 2 doses of maintenance therapy or at least 2 doses of a second induction course); **OR**
3. T1 disease (i.e., tumor has spread to the connective tissue, but not the muscle) following a single induction course of BCG; **AND**

B. Individual is ineligible for cystectomy; **AND**

C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**

D. Individual has a current ECOG performance status of 0-2; **AND**

E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

LXI. Individual has a diagnosis of advanced, recurrent, or metastatic vulvar cancer;

A. Individual is using as a single agent; **AND**

B. Individual has a tumor with PD-L1 gene expression with Combined Positive Score (CPS) of greater than or equal to 1 (CPS ≥ 1); **AND**

C. Individual has disease progression on or after chemotherapy; **AND**

D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

***Note:** Actionable molecular markers include EGFR, ALK, ROS1, BRAF, NTRK, MET and RET mutations. The NCCN panel recommends testing prior to initiating therapy to help guide appropriate treatment. If there is insufficient tissue to allow testing for all of these markers, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes (NCCN 1, 2A).

Keytruda (pembrolizumab) may not be approved when the above criteria are not met and for all other indications.

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    i. Cervical Cancer. V2.2024. Revised February 23, 2024.
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    p. Head and Neck Cancer V3.2024. Revised February 29, 2024.
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    dd. Pediatric Hodgkin Lymphoma. V2.2023. March 9, 2023.
    ee. Penile Cancer V1.2024. Revised October 25, 2023.
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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.