SmartHealth

Ascension

Pembrolizumab

(Keytruda®) J9271

Covered with prior authorization

Pembrolizumab (Keytruda®) may be authorized when the following criteria are met:

- Prescriber is an oncology practitioner.

AND

- For a FDA-approved indication or indication supported by national guidelines, such as National Comprehensive Cancer Network (NCCN).

AND

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

AND

- Diagnosis of locoregional unresectable or metastatic Adrenocortical Carcinoma; **AND**
- Individual is using as single agent, or in combination with mitotane; **AND**
- Individual has a current ECOG performance status of 0-2; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent**.**

OR

- Diagnosis of locally recurrent, unresectable, or metastatic Triple-Negative Breast Cancer (TNBC); **AND**
- Individual is using in combination with paclitaxel/nab-paclitaxel, or in combination with gemcitabine and a platinum agent); **AND**
- Individual has a tumor with PD-L1 gene expression with Combined Positive Score (CPS) of greater than or equal to 10; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current Eastern Cooperative Group (ECOG) performance status of 0-2.

OR

- Diagnosis of high risk early-stage Triple-Negative Breast Cancer (TNBC); **AND**
- Individual is using in combination with chemotherapy in the neoadjuvant setting; **AND**
- Individual will continue/is continuing Keytruda® as single agent in the adjuvant setting after surgical intervention; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current Eastern Cooperative Group (ECOG) performance status of 0-2.

OR

- Diagnosis of persistent, recurrent or metastatic Cervical Cancer; **AND**

Developed by: Medical Specialty Prior Authorization Team, April 2022
Approved by: Ambulatory Care Expert Review Panel, April 2022; Therapeutic Affinity Group, May 2022

- Individual is using in combination with paclitaxel and a platinum agent, with or without bevacizumab; **AND**
- Individual has a tumor with PD-L1 gene expression with Combined Positive Score (CPS) of greater than or equal to 1 (CPS ≥ 1); **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current Eastern Cooperative Group (ECOG) performance status of 0-2.

OR

- Diagnosis of recurrent or metastatic Cervical Cancer; **AND**
- Individual is using as monotherapy; **AND**
- Individual has a tumor with PD-L1 gene expression with Combined Positive Score (CPS) of greater than or equal to 1; **AND**
- Individual has not received treatment with another anti-PD-1 agent; **AND**
- Individual has a current Eastern Cooperative Group (ECOG) performance status of 0-2.

OR

- Diagnosis of Colorectal Cancer **AND**
- Individual is using as monotherapy; **AND**
- Individual meets **one** of the following:
    - Primary treatment as a single agent for unresectable metachronous metastases (deficient mismatch repair/high microsatellite instability [dMMR/MSI-H] only) and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months**; OR**
    - Subsequent therapy as a single agent (if nivolumab or pembrolizumab not previously given) for unresectable advanced or metastatic disease (dMMR/MSIH only) following previous treatment with **one** of the following: Oxaliplatin-, irinotecan-, and/or fluoropyrimidine-based therapy**; OR**
    - First line treatment as a single agent for unresectable or metastatic disease (dMMR/MSIH only)**; AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of locally advanced, recurrent or metastatic Cutaneous Squamous Cell Carcinoma (cSCC); **AND**
- Individual is using as monotherapy; **AND**
- Disease is not curable by surgery or radiation; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of advanced Endometrial Cancer (not dMMR/MSI-H); **AND**
- Individual is using in combination with lenvatinib; **AND**

- Individual has confirmed disease progression after one or more prior lines of systemic therapy; **AND**
- Individual is not a candidate for curative surgery or radiation; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of recurrent locally advanced or metastatic squamous cell Esophageal Cancer; **AND**
- Individual is using as monotherapy; **AND**
- Individual has a tumor with PD-L1 gene expression with CPS of greater than or equal to 10; **AND**
- Individual has demonstrated disease progression after one or more prior lines of systemic therapy; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of unresectable, recurrent locally advanced, or metastatic Esophageal Cancer; **AND**
- Individual is using in combination with platinum and fluoropyrimidine-based chemotherapy; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of recurrent locally advanced or metastatic Gastric or Gastroesophageal Junction Adenocarcinoma; **AND**
- Individual is using as monotherapy; **AND**
- Individual has a tumor with PD-L1 gene expression with CPS of greater than or equal to 1; **AND**
- 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**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of locally advanced unresectable or metastatic Gastric or Gastroesophageal Junction Adenocarcinoma; **AND**
- Individual has HER2-positive disease and is using as first line treatment; **AND**
- Individual is using in combination with trastuzumab, platinum- and fluoropyrimidine-based chemotherapy; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of recurrent, unresectable, or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC); **AND**

- Individual is using as monotherapy; **AND**
- Individual meets **one** of the following:
    - Individual is using as first-line treatment for tumor with PD-L1 gene expression with CPS of greater than or equal to 1; **OR**
    - Individual has demonstrated disease progression on or after platinum-containing chemotherapy; **OR**
    - Individual is using as first-line treatment in combination with platinum-containing chemotherapy and fluorouracil regardless of PD-L1 expression; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of Hepatocellular Carcinoma (HCC); **AND**
- Individual has Child-Pugh Class A advanced HCC; **AND**
- Individual is using as monotherapy; **AND**
- Individual has demonstrated disease progression or intolerance on or after treatment with an approved first-line agent; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of relapsed or refractory Hodgkin Lymphoma except for those with lymphocyte-predominant Hodgkin lymphoma.

OR

- Diagnosis of Malignant Pleural Mesothelioma; **AND**
- Individual is using as subsequent therapy; **OR**
- Individual is ineligible for platinum-based chemotherapy, defined as having **one or more** of the following risk factors for platinum-based chemotherapy toxicity:
    - ECOG performance status equal to 2**; OR**
    - Glomerular filtration rate less than 60 mL/min**; OR**
    - Hearing loss (measured at audiometry) of 25 dB at two contiguous frequencies**; OR**
    - Grade 2 or greater peripheral neuropathy; **AND**
- Individual is using as monotherapy; **AND**
- Individual has a current ECOG performance status of 0-2; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Melanoma (cutaneous and uveal); **AND**
- Individual has confirmed presence of unresectable or metastatic melanoma; **AND**
- Individual is using as monotherapy; **AND**
- Individual meets **one** of the following:
    - Individual is using as first-line therapy in untreated disease; **OR**

    - Individual is using as second-line or subsequent therapy for confirmed disease progression while receiving or since completing most recent therapy; **AND**
- Individual has current ECOG performance status of 0-2; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Melanoma (cutaneous and uveal); **AND**
- Individual has resected, stage IIB, IIC or high-risk stage III disease; **AND**
- Individual is using as monotherapy; **AND**
- Individual is using as adjuvant therapy for up to 12 months; **AND**
- Individual has a current ECOG performance status of 0-2; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of metastatic Melanoma with brain metastases; **AND**
- Individual has a primary diagnosis of melanoma; **AND**
- Individual is using as single agent for brain metastases**; AND**
- Individual has a current ECOG performance status of 0-2; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Merkel Cell Carcinoma (MCC); **AND**
- Individual is using as monotherapy; **AND**
- Individual has presence of metastatic or advanced locoregional MCC determined to be not amenable to definitive surgery or radiation therapy; **AND**
- Individual has a current ECOG performance status of 0-2; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Non-Hodgkin Lymphoma, Primary Mediastinal Large B-Cell Lymphoma; **AND** Individual is using as monotherapy; **AND**
- Individual is using to treat refractory disease or subsequent therapy for disease relapse after receiving two or more prior lines of therapy; **AND**
- Individual has a current ECOG performance status of 0-2; **AND,**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of advanced, recurrent, or metastatic Non-Small Cell Lung Cancer (NSCLC); **AND**
- Individual is using for the first-line treatment; **AND**
- Individual's disease is confirmed cytologically as stage III or IV NSCLC; **AND**
- Individual is using as monotherapy; **AND**
- Confirmation tumor expresses PD-L1 gene on at least 1% or greater of tumor cells; **AND**
- Individual does not have presence of actionable molecular markers; **AND**

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

OR

- Diagnosis of advanced, recurrent, or metastatic non squamous NSCLC; **AND**
- Individual is using for first-line treatment; **AND**
- Disease is confirmed cytologically as stage IIIb or IV NSCLC; **AND**
- Individual is using in combination with pemetrexed and a platinum agent; **AND**
- Individual does not have presence of actionable molecular markers; **AND**
- 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**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of advanced, recurrent, or metastatic squamous NSCLC; **AND**
- Individual is using for first line treatment; **AND**
- Disease is confirmed cytologically as stage IV NSCLC; **AND**
- Individual is using in combination with carboplatin plus paclitaxel or nab-paclitaxel; **AND**
- Individual does not have presence of actionable molecular markers; **AND**
- 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**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of advanced, recurrent or metastatic nonsquamous NSCLC; **AND**
- 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**
- Individual has confirmed achievement of tumor response or stable disease following initial cytotoxic therapy; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of advanced, recurrent, or metastatic squamous cell NSCLC; **AND**
- Individual is using as monotherapy as continuation maintenance therapy, if given first-line as part of pembrolizumab/carboplatin/paclitaxel (or nab-paclitaxel) regimen; **AND**
- Individual has confirmed achievement of tumor response or stable disease following initial cytotoxic therapy; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of advanced, recurrent, metastatic NSCLC; **AND**

- Individual is using as monotherapy in second or subsequent line of therapy; **AND**
- Individual has confirmed tumor with PD-L1 gene expression level greater than or equal to 1% with disease progression on or after platinum-containing chemotherapy; **AND**
- If Individual has anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) genomic tumor aberrations present, they must have confirmed disease progression on U.S. Food and Drug Administration (FDA) approved therapy for the aberrations prior to receiving pembrolizumab (Keytruda®); **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of metastatic NSCLC with brain metastases; **AND**
- Individual has a primary diagnosis of non-small cell lung cancer; **AND**
- Individual is using as single agent for brain metastases; **AND**
- Individual has confirmed tumor with PD-L1 gene expression level greater than or equal to 1%; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2

OR

- Diagnosis of advanced Renal Cell Carcinoma (RCC); **AND**
- Individual has histological confirmation of RCC with clear cell component; **AND**
- Individual is using as first-line therapy; **AND**
- Individual is using in combination with axitinib or lenvatinib; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current Karnofsky performance status of ≥ 70%.

OR

- Diagnosis of Renal Cell Carcinoma (RCC); **AND**
- Individual is using as adjuvant treatment for intermediate-high or high risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions; **AND**
- Individual has not received treatment with another PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of unresectable, recurrent, advanced, or metastatic Soft Tissue Sarcoma; **AND**
- Individual is using as monotherapy for first line or subsequent therapy; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of unresectable or metastatic solid tumors (dMMR/MSIH only); **AND**
- Individual is using as monotherapy; **AND**

- Individual has confirmed disease progression following prior treatment with no other satisfactory alternative treatment options; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of unresectable or metastatic solid tumors; **AND**
- Individual is using as monotherapy; **AND**
- Individual has high tumor mutation burden (TMB) (greater than or equal to 10 mutations per megabase) with test results confirmed; **AND**
- Individual has confirmed disease progression following prior treatment with no other satisfactory alternative treatment options; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of unresectable or metastatic Thymic Carcinoma; **AND**
- Individual is using as monotherapy; **AND**
- Individual has confirmed disease progression following chemotherapy, or intolerance to first-line combination regimens; **AND**
- Individual does not have thymomas; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of locally advanced or metastatic Urothelial Carcinoma; **AND**
- Individual is using as monotherapy; **AND**
- Individual meets **one** of the following:
    - Individual is not eligible for any platinum-containing chemotherapy; **OR**
    - Individual is using as subsequent therapy; **OR**
    - Individual has confirmed disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum containing chemotherapy; **AND**
- Individual has not received treatment with another anti PD-1 or anti-PD-L1 agent**; AND**
- Individual has a current ECOG performance status of 0-2.

OR

- 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; **AND**
- Individual has Bacillus Calmette-Guerin (BCG)-unresponsive disease defined as **one** of the following:
    - 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**

    - 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**
    - T1 disease (i.e., tumor has spread to the connective tissue, but not the muscle) following a single induction course of BCG; **AND**
- Individual is ineligible for cystectomy; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

AND

- Dosing by indication is supported by FDA or national standard of care protocols at the time the request is submitted:
    - Melanoma: 200 mg every 3 weeks or 400 mg every 6 weeks
    - NSCLC: 200 mg every 3 weeks or 400 mg every 6 weeks
    - SCLC: 200 mg every 3 weeks or 400 mg every 6 weeks
    - HNSCC: 200 mg every 3 weeks or 400 mg every 6 weeks
    - cHL or PMBCL: 200 mg every 3 weeks or 400 mg every 6 weeks for adults; 2 mg/kg (up to 200 mg) every 3 weeks for pediatrics
    - Urothelial Carcinoma: 200 mg every 3 weeks or 400 mg every 6 weeks
    - MSI-H or dMMR Cancer: 200 mg every 3 weeks or 400 mg every 6 weeks for adults; 2 mg/kg (up to 200 mg) every 3 weeks for pediatrics
    - MSI-H or dMMR CRC: 200 mg every 3 weeks or 400 mg every 6 weeks
    - Gastric Cancer: 200 mg every 3 weeks or 400 mg every 6 weeks
    - Esophageal Cancer: 200 mg every 3 weeks or 400 mg every 6 weeks
    - Cervical Cancer: 200 mg every 3 weeks or 400 mg every 6 weeks
    - HCC: 200 mg every 3 weeks or 400 mg every 6 weeks
    - MCC: 200 mg every 3 weeks or 400 mg every 6 weeks for adults; 2 mg/kg (up to 200 mg) every 3 weeks for pediatrics
    - RCC: 200 mg every 3 weeks or 400 mg every 6 weeks with axitinib 5 mg orally twice daily
    - Endometrial Carcinoma: 200 mg every 3 weeks or 400 mg every 6 weeks with lenvatinib 20 mg orally once daily for tumors that are not MSI-H or dMMR
    - TMB-H Cancer:
        - 200 mg every 3 weeks or 400 mg every 6 weeks for adults
        - 2 mg/kg (up to 200 mg) every 3 weeks for pediatrics
    - cSCC: 200 mg every 3 weeks or 400 mg every 6 weeks
    - TNBC: 200 mg every 3 weeks or 400 mg every 6 weeks

Exclusion criteria:

- Keytruda® (pembrolizumab) may not be approved when the above criteria are not met and for all other indications;
- Doses, durations, or dosing intervals that exceed FDA maximum limits for any FDA-approved indication or are not supported by industry-accepted practice guidelines or peer-reviewed literature for the relevant off-label use;
- Individuals with significant known risk factors unless the record provides an assessment of clinical benefit that outweighs the risk.

Initial authorization is up to 12 months.

Continuation requests may be approved if there is confirmation of clinically significant improvement or stabilization in clinical signs and symptoms of the disease. Clinical documentation provided must be from within the most recent 12 months.

Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

U.S. Food and Drug Administration:
This section is to be used for informational purposes. FDA approval alone is not a basis for coverage

Keytruda® is a programmed death receptor-1 (PD-1)-blocking antibody with the following approved indications:

- Melanoma
- Non-Small Cell Lung Cancer (NSCLC)
- Small Cell Lung Cancer (SCLC)
- Head and Neck Squamous Cell Cancer (HNSCC)
- Classical Hodgkin Lymphoma (cHL)
- Primary Mediastinal Large B-Cell Lymphoma (PMBCL)
- Urothelial Carcinoma
- Microsatellite Instability-High or Mismatch Repair Deficient Cancer (MSI-H) (dMMR)
- Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer (CRC)
- Gastric Cancer
- Esophageal Cancer
- Cervical Cancer
- Hepatocellular Carcinoma (HCC)
- Merkel Cell Carcinoma (MCC)
- Renal Cell Carcinoma (RCC)
- Endometrial Carcinoma
- Tumor Mutational Burden-High (TMB-H) Cancer
- Cutaneous Squamous Cell Carcinoma (cSCC)
- Triple-Negative Breast Cancer (TNBC)

References:

Ascension Hematology and Oncology Expert Review Panel. (2021, April 22). *Pembrolizumab and Nivolumab Clinical Opportunities*. Ascension TAG INITIATIVES-PSWP.
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Merck. (2022). *Keytruda® (pembrolizumab)* [prescribing information]. Kenilworth, NJ. https://www.keytruda.com

Pembrolizumab (Keytruda®). (2020-2022). National Comprehensive Cancer Network, Inc. (Copyright © National Comprehensive Cancer Network, Inc). *NCCN Guidelines: Treatment by Cancer Type*. NCCN Clinical Practice Guidelines in Oncology. Retrieved April 25, 2022, from https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type

Criteria History/ Revision Information:

Date	Summary of Changes
April 2021	Pembrolizumab and Nivolumab Clinical Opportunities developed by Ascension Hematology and Oncology Expert Review Panel
May 2021	Approved by Therapeutic Affinity Group
April 2022	Criteria for use summary developed by Ascension Medical Specialty Prior Authorization Team
May 2022	Criteria for use summary approved by Ascension Therapeutic Affinity Group

If you have questions, call 833-980-2352 to speak to a member of the Ascension Rx prior authorization team or email your questions to smarthealthspecialty@ascension.org.