SmartHealth

Ascension

Nivolumab

(Opdivo®) J9299

Covered with prior authorization

Nivolumab (Opdivo®) 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 Colorectal Cancer; **AND**
- Individual meets **one** of the following criteria:
    - Individual is using in primary treatment for unresectable metachronous metastases (defective 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
        - as monotherapy; **OR**
        - in combination with ipilimumab; **OR**
    - Individual is using as subsequent therapy for unresectable advanced or metastatic disease (defective mismatch repair/ high microsatellite instability [[dMMR/MSI-H] only) following previous treatment with fluoropyrimidine-, oxaliplatin-, or irinotecan- based chemotherapy;
        - as monotherapy; **OR**
        - In combination with ipilimumab; **AND**
- Individual has not received another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual has a current ECOG performance status of 0-2.

OR

- Diagnosis of unresectable locally advanced, recurrent, or metastatic Esophageal Squamous Cell Carcinoma (ESCC); **AND**
- Individual is using as single agent for second line or subsequent therapy; **AND**
- Individual has confirmation of disease progression on or had intolerance to fluoropyrimidine- and platinum-based chemotherapy; **AND**
- Individual has a current ECOG performance status of 0-2 or Karnofsky performance score of 60-100; **AND**
- Individual has not received treatment with another anti-PD-1, anti-PD-L1 agent, or other checkpoint inhibitor.

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

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OR

- Diagnosis of completely resected Esophageal or Gastroesophageal Junction Cancer; **AND**
- Individual is using as single agent for residual pathologic disease; **AND**
- Individual has received neoadjuvant chemoradiotherapy (CRT); **AND**
- Individual has a current ECOG performance status of 0-2; **AND**
- Individual has not received treatment with another anti-PD-1, anti-PD-L1 agent, or other checkpoint inhibitor.

OR

- Diagnosis of advanced or metastatic Gastric, Gastroesophageal Junction Cancer, or Esophageal Adenocarcinoma; **AND**
- Individual is using in combination with fluoropyrimidine and platinum-containing chemotherapy; **AND**
- Individual has a current ECOG performance status of 0-2; **AND**
- Individual has not received treatment with another anti-PD-1, anti-PD-L1 agent, or other checkpoint inhibitor.

OR

- Diagnosis of advanced Hepatocellular Carcinoma; **AND**
- Individual is using in combination with ipilimumab for subsequent 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-1 agent.

OR

- Diagnosis of Hodgkin Lymphoma; **AND**
- Individual is using for relapsed or refractory Hodgkin lymphoma except for those with lymphocyte-predominant Hodgkin lymphoma.

OR

- Diagnosis of unresectable Malignant Pleural or Peritoneal Mesothelioma; **AND**
- Using as first line therapy; **AND**
- Individual is using in combination with ipilimumab (Yervoy); **AND**
- Individual has a ECOG performance status of 0-2; **AND**
- Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Malignant Pleural or Peritoneal Mesothelioma; **AND**
    - Individual is using as a single agent, **OR**
    - In combination with ipilimumab (Yervoy) for subsequent therapy; **AND**
- Individual has a ECOG performance status of 0-2; **AND**
- Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Melanoma (Cutaneous or Uveal); **AND**
- Individual has unresectable or metastatic melanoma; **AND**
- **One** of the following:
    - Using as first-line therapy for untreated melanoma
        - as a single agent; **OR**
        - in combination with ipilimumab; **OR**

    - Using as second-line or subsequent therapy for confirmed disease progression while receiving or since completing most recent therapy
        - as a single agent; **OR**
        - in combination with ipilimumab; **AND**
- Current ECOG performance status of 0-2; **AND**
- Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of resected advanced melanoma; **AND**
- Individual is using as a single agent for up to 12 months of adjuvant therapy; **AND**
- Individual has resected stage IIIB, IIIC, or stage IV disease; **AND**
- Current ECOG performance status of 0-2; **AND**
- 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 has asymptomatic brain metastases; **AND**
    - Individual is using as monotherapy or in combination with ipilimumab; **AND**
    - Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

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

OR

- Diagnosis of Non-Small Cell Lung Cancer (NSCLC) and the following criteria are met:
- Individual has metastatic NSCLC; **AND**
- Individual is using as a single agent; **AND**
- Confirmation of disease progression on or after platinum-containing chemotherapy; **AND**
- Current ECOG performance status of 0-2; **AND**
- Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
- Individual is not receiving therapy for an autoimmune disease, chronic condition, or interstitial lung disease with a systemic immunosuppressant.

OR

- Diagnosis of recurrent, advanced, or metastatic NSCLC; **AND**
- Using as first-line therapy; **AND**
- Individual is using in combination with ipilimumab; **AND**
- Individual does not have presence of actionable molecular markers; **AND**
- Current ECOG performance status of 0-2; **AND**
- Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of recurrent or metastatic NSCLC; **AND**
- Using as first-line therapy; **AND**

- Individual is using in combination with ipilimumab *and* 2 (two) cycles of platinum-doublet chemotherapy (i.e., platinum-based chemotherapy with pemetrexed, or carboplatin with paclitaxel); **AND**
- Individual does not have presence of actionable molecular markers; **AND**
- Current ECOG performance status of 0-2; **AND** Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

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 PD-L1 expression positive (≥ 1%) tumors; **AND**
- Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Renal Cell Carcinoma (RCC); **AND**
- Individual has **advanced or metastatic** RCC; **AND**
    - Individual is using as monotherapy; **AND**
    - Histological confirmation of RCC with clear-cell component; **AND**
    - Individual has confirmation of disease progression after one or two prior anti-angiogenic regimens (e.g. axitinib, bevacizumab [or bevacizumab biosimilar], pazopanib, sorafenib, sunitinib, etc.) for treatment of advanced or metastatic disease; **AND**
    - Current ECOG performance status of 0-2; **AND**
    - Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **OR**
- Individual has **intermediate- or poor-risk, advanced** RCC; **AND**
    - Using as first-line therapy for previously untreated RCC in combination with ipilimumab for four cycles followed by single agent Opivido® (nivolumab); **OR**
    - Using as subsequent therapy, if no checkpoint blockade (PD-1, PD-L1, or CTLA-4) antibody treatment has been previously administered in combination with ipilimumab for four cycles followed by single agent Opivido® (nivolumab); **AND**
    - Histological confirmation of RCC with clear-cell component; **AND**
    - Current ECOG performance status of 0-2; **AND**
    - Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **OR**
- Individual has **relapsed, recurrent, or advanced** RCC; **AND**
    - Individual is using as first-line therapy in combination with cabozantinib tablets; **AND**
    - Current ECOG performance status of 0-2; **AND**
    - Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Small Bowel Adenocarcinoma (SBA); **AND**
    - Individual has advanced or metastatic disease (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] only); **AND**
    - Individual is using subsequent therapy
        - As monotherapy; OR
        - In combination with ipilimumab; **AND**
    - Current ECOG performance status of 0-2; **AND**
    - Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Small Bowel Adenocarcinoma (SBA): Advanced ampullary cancer; **AND**
  - Individual has advanced or metastatic disease (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] only); **AND**
  - Individual is using as initial or subsequent therapy
    - As monotherapy; **OR**
    - in combination with ipilimumab; **AND**
  - Current ECOG performance status of 0-2; **AND**
  - Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Squamous Cell Carcinoma of the Head and Neck (SCCHN); **AND**
  - Individual has recurrent, unresectable, or metastatic SCCHN; **AND**
  - Individual is using as monotherapy; **AND**
  - Individual has confirmation of disease progression on or after platinum-containing chemotherapy; **AND**
  - Current ECOG performance status of 0-2; **AND**
  - Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

OR

- Diagnosis of Urothelial carcinoma; **AND**
  - Individual has locally advanced or metastatic disease;
    AND
  - Individual is using as a single agent; **AND**
  - Meets **one** of the following:
    - Confirmation of disease progression on or after platinum-containing chemotherapy; **OR**
    - Confirmation of disease progression within 12 months of receiving neoadjuvant or adjuvant treatment with platinum-containing chemotherapy;

    OR
  - Individual is using as single agent for adjuvant therapy; **AND**
  - Individual is at high risk of recurrence after having radical resection; **AND**
- Current ECOG performance status of 0-2; **AND**
- Has not received treatment with another anti-PD-1 or anti-PD-L1 agent.

AND

- Dosing by indication is supported by FDA or national standard of care protocols at the time the request is submitted:
  - Unresectable or metastatic melanoma
    - 240 mg every 2 weeks or 480 mg every 4 weeks
    - 1 mg/kg followed by ipilimumab 3 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks
  - Adjuvant treatment of melanoma
    - 240 mg every 2 weeks or 480 mg every 4 weeks
  - Neoadjuvant treatment of resectable (tumors ≥4 cm or node positive) non small cell lung cancer
    - 360 mg with platinum-doublet chemotherapy on the same day every 3 weeks for 3 cycles (2.2)
  - Metastatic non-small cell lung cancer

        - 3 mg/kg every 2 weeks with ipilimumab 1 mg/kg every 6 weeks
        - 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks and 2 cycles of platinum-doublet chemotherapy
        - 240 mg every 2 weeks or 480 mg every 4 weeks
    - Malignant pleural mesothelioma
        - 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks
    - Advanced renal cell carcinoma
        - 3 mg/kg followed by ipilimumab 1 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks
        - 240 mg every 2 weeks or 480 mg every 4 weeks administered in combination with cabozantinib 40 mg once daily without food
        - 240 mg every 2 weeks or 480 mg every 4 weeks
    - Classical Hodgkin lymphoma
        - 240 mg every 2 weeks or 480 mg every 4 weeks
    - Recurrent or metastatic squamous cell carcinoma of the head and neck
        - 240 mg every 2 weeks or 480 mg every 4 weeks
    - Adjuvant treatment of urothelial carcinoma
        - 240 mg every 2 weeks or 480 mg every 4 weeks
    - Locally advanced or metastatic urothelial carcinoma
        - 240 mg every 2 weeks or 480 mg every 4 weeks
    - Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer
        - Adult and pediatric patients ≥ 40 kg: 240 mg every 2 weeks or 480 mg every 4 weeks
        - Pediatric patients < 40 kg: 3 mg/kg every 2 weeks
        - Adult and pediatric patients ≥ 40 kg: 3 mg/kg followed by ipilimumab 1 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks
    - Hepatocellular carcinoma
        - 1 mg/kg followed by ipilimumab 3 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks
    - Adjuvant treatment of resected esophageal or gastroesophageal cancer
        - 240 mg every 2 weeks or 480 mg every 4 weeks for 16 weeks, then 480 mg every 4 weeks for total treatment duration of 1 year
    - Esophageal squamous cell carcinoma
        - 240 mg every 2 weeks or 480 mg every 4 weeks
    - Gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma (GC, GEJC, or EAC)
        - 360 mg every 3 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 3 weeks
        - 240 mg every 2 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 2 weeks

Exclusion criteria:

Requests may not be approved for the following:

- Opivido® (Nivolumab) 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.

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

Opivido® is a programmed death receptor-1 (PD-1)-blocking antibody and has the following FDA approved indications:

- Melanoma
- Non-Small Cell Lung Cancer (NSCLC)
- Malignant Pleural Mesothelioma
- Renal Cell Carcinoma (RCC)
- Classical Hodgkin Lymphoma (cHL)
- Squamous Cell Carcinoma of the Head and Neck (SCCHN)
- Urothelial Carcinoma
- Colorectal Cancer
- Hepatocellular Carcinoma (HCC)
- Esophageal Cancer
- Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma

References:

Ascension Hematology and Oncology Expert Review Panel. (2021, April 22). *Pembrolizumab and Nivolumab Clinical Opportunities*. Ascension TAG INITIATIVES-PSWP.
Bristol-Myers-Squibb. (2021). *Opivido® (nivolumab)* [prescribing information]. New York, NY. https://www.opdivo.com
Nivolumab (Opivido®). (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
OPDIVO® (nivolumab) Label. (2022, March). Accessdata.fda.gov. Retrieved April 23, 2022, from https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/225554s112lbl.pdf

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.