Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

Opdivo (nivolumab)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Opdivo (nivolumab)

APPROVAL CRITERIA

Requests for Opdivo (nivolumab) may be approved if the following criteria are met:

I. Individual has a diagnosis of Colorectal Cancer and **one** of the following is met (Label, NCCN 2A):
   A. Individual is using as monotherapy or in combination with ipilimumab in primary treatment for unresectable metachronous metastases (defective 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**
   B. Individual is using as monotherapy or in combination with ipilimumab as subsequent therapy for unresectable advanced or metastatic disease (defective mismatch repair/high microsatellite instability [dMMR/MSIH] only) following previous treatment with fluoropyrimidine-, oxaliplatin-, or irinotecan- based chemotherapy;

AND

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

III. Individual has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0-2; **AND**

IV. 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 advanced Hepatocellular Carcinoma and the following criteria are met:
   A. Individual is using as monotherapy or in combination with ipilimumab; **AND**
   B. Individual has confirmation of disease progression on or had intolerance to sorafenib; **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**

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

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 Hodgkin Lymphoma and the following criterion is met (Label, NCCN 2A):
   A. Individual is using for relapsed or refractory Hodgkin lymphoma except for those with lymphocyte-predominant Hodgkin lymphoma;

OR

VII. Individual has a diagnosis of Malignant Pleural Mesothelioma and the following criteria are met (NCCN 2A):
   A. Individual is using as subsequent therapy; **OR**
   B. Individual is ineligible for platinum-based chemotherapy, defined as having one or more of the following risk factors for platinum-based toxicity:
      1. ECOG performance status equal to 2;
      2. Glomerular filtration rate less than 60 mL/min;
      3. Hearing loss (measured at audiometry) of 25 dB at two contiguous frequencies;
      4. Grade 2 or greater peripheral neuropathy;

   AND

   C. Individual is using as monotherapy; **AND**
   D. Individual has a 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

VIII. Individual is using for the treatment of Malignant Pleural Mesothelioma (NCCN 2A); **AND**
   A. Individual is using in combination with ipilimumab (Yervoy) for subsequent therapy; **AND**
   B. Individual has a ECOG performance status of 0-2; **AND**
   C. 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

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

IX. Individual has a diagnosis of Melanoma (Cutaneous or Uveal) when the following criteria are met:
  A. Individual has unresectable or metastatic melanoma; **AND**
    1. Individual is using as a single agent, or in combination with ipilimumab as first-line therapy for untreated melanoma; **OR**
    2. Individual is using as a single agent, or in combination with ipilimumab as second-line or subsequent therapy for confirmed disease progression while receiving or since completing most recent therapy, if anti-PD-1 or anti-PD-L1 not previously used; **AND**
    3. Individual has a current ECOG performance status of 0-2; **AND**
    4. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
    5. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

  OR

  B. Individual has resected advanced melanoma (Label, NCCN 2A); **AND**
    1. Individual is using as a single agent for up to 12 months of adjuvant therapy; **AND**
    2. Individual has resected stage IIIB, IIIC, or stage IV disease; **AND**
    3. Individual has a current ECOG performance status of 0-2; **AND**
    4. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
    5. 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 metastatic Melanoma with brain metastases and the following criteria are met (NCCN 2A):
  A. Individual has a primary diagnosis of melanoma; **AND**
  B. Individual has asymptomatic brain metastases (Long 2017, 2018, Tawbi 2017); **AND**
  C. Individual is using as monotherapy or in combination with ipilimumab; **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

XI. Individual has a diagnosis of Merkel Cell Carcinoma and the following criteria are met:
  A. Individual is using as a single agent; **AND**
  B. Individual has presence of metastatic or recurrent locoregional MCC determined to

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

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

XII. Individual has a diagnosis of Non-Small Cell Lung Cancer (NSCLC) and the following criteria are met:

A. Individual has metastatic NSCLC; **AND**

1. Individual is using as a single agent; **AND**
2. Individual has confirmation of disease progression on or after platinum-containing chemotherapy; **AND**
3. Individual has a current ECOG performance status of 0-2; **AND**
4. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
5. Individual is not receiving therapy for an autoimmune disease, chronic condition or interstitial lung disease with a systemic immunosuppressant;

OR

B. Individual has stage IV or recurrent NSCLC and using as first line therapy (Label, NCCN 2A); **AND**

1. Individual is using in combination with ipilimumab; **AND**
2. Cytologically confirmed stage IV or recurrent NSCLC; **AND**
3. Individual has high tumor mutation burden (greater than or equal to 10 mutations per megabase); **AND**
4. Individual does not have sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) translations in nonsquamous carcinoma; **AND**
5. Individual has not received prior systemic therapy as primary therapy for advanced or metastatic NSCLC; prior adjuvant or neoadjuvant chemotherapy is permitted as long as the last administration of the prior regimen occurred at least 6 months prior; **AND**
6. Current ECOG performance status of 0-2; **AND**
7. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
8. Individual is not receiving therapy for an autoimmune disease, chronic condition or interstitial lung disease with a systemic immunosuppressant;

OR

C. Individual has recurrent, advanced, or metastatic NSCLC and using as first-line

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

therapy (Label, NCCN 2A); **AND**

1. Individual is using in combination with ipilimumab; **AND**
2. Individual does not have presence of EGFR, ALK, ROS1, or BRAF mutations; **AND**
3. Current ECOG performance status of 0-2; **AND**
4. Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
5. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

D. Individual has recurrent or metastatic NSCLC and using as first-line therapy; **AND**

1. 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**
2. Individual does not have presence of EGFR, ALK, ROS1, or BRAF mutations; **AND**
3. Current ECOG performance status of 0-2; **AND**
4. Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
5. 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 Renal Cell Carcinoma (RCC) (Label, NCCN 2A); **AND**

A. Individual has advanced or metastatic RCC ; **AND**

1. Individual is using as monotherapy; **AND**
2. Histologic confirmation of RCC with clear-cell component; **AND**
3. Individual has confirmation of disease progression after one or two prior anti-angiogenic regimens (for example, axitinib, bevacizumab [or bevacizumab biosimilar], pazopanib, sorafenib, sunitinib, etc.) for treatment of advanced or metastatic disease; **AND**
4. Individual has a current ECOG performance status 0-2; **AND**
5. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
6. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with an immunosuppressant;

OR

B. Individual has intermediate- or poor-risk, advanced RCC; **AND**

1. Individual is using in combination with ipilimumab , for four cycles followed by single agent Opdivo (nivolumab) as first-line therapy for previously untreated RCC; **OR**

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

2. Individual is using in combination with ipilimumab for four cycles followed by single agent Opdivo (nivolumab), as subsequent therapy, if no checkpoint blockade (PD-1, PD-L1, or CTLA-4) antibody treatment has been previously administered (NCCN 2A);

AND

3. Histologic confirmation of RCC with clear-cell component; **AND**
4. Individual has a current ECOG performance status 0-2; **AND**
5. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
6. 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 Small Bowel Adenocarcinoma (SBA) and meets the following criteria (NCCN 2A):

A. Individual has advanced or metastatic disease (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] only); **AND**
B. Individual is using as monotherapy or in combination with ipilimumab as subsequent therapy; **AND**
C. Current ECOG performance status of 0-2; **AND**
D. 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

XV. Individual has a diagnosis of Small Cell Lung Cancer (SCLC) and meets the following criteria (Label, NCCN 2A):

A. Individual is using as monotherapy, or in combination with ipilimumab, as subsequent therapy and individual meets one of the following:
   1. Demonstrated disease relapse within 6 months following complete or partial response or stable disease with initial treatment; **OR**
   2. No response with initial treatment; **OR**
   3. Primary progressive disease;

   AND

   4. Individual has a current ECOG performance status of 0-2; **AND**
   5. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   6. Individual is not receiving therapy for an autoimmune disease, chronic condition or interstitial lung disease with a systemic immunosuppressant;

OR

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

XVI. Individual has a diagnosis of Squamous Cell Carcinoma of the Head and Neck (SCCHN) and meet the following criteria:
- A. Individual has recurrent, unresectable, or metastatic SCCHN; **AND**
  1. Individual is using as monotherapy; **AND**
  2. Individual has confirmation of disease progression on or after platinum-containing chemotherapy; **AND**
  3. Individual has a current ECOG performance status of 0-2; **AND**
  4. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
  5. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XVII. Individual has Urothelial carcinoma and meets the following criteria:
- A. Individual has locally advanced or metastatic disease; **AND**
- B. Individual is using as a single agent; **AND**
- C. Individual meets the following criteria:
  1. Confirmation of disease progression on or after platinum-containing chemotherapy; **OR**
  2. Confirmation of disease progression within 12 months of receiving neoadjuvant or adjuvant treatment with platinum-containing chemotherapy;

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

Requests for Opdivo (nivolumab) may not be approved when the above criteria are not met and for all other indications.

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1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2019. URL: http://www.clinicalpharmacology.com. Updated periodically.
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4. Hellmann MD, Ciuleanu TE, Pluzanski A, et al. Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden. N Engl J Med. 2018; 378(22):2093-2104.

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

5. Hellmann MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. *N Eng J Med.* 2019;381:2020-31.
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7. Long GV, Atkinson V, Lo S, et al. Combination nivolumab and ipilimumab or nivolumab alone in melanoma brain metastases: a multicenter randomized phase 2 study. *Lancet Oncol.* 2018;19:672-81.
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9. NCCN Clinical Practice Guidelines in Oncology™. © 2020 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on May 28, 2020.
    a. Anal Carcinoma V1.2020. Revised November 19, 2019.
    b. Bladder Cancer V1.2020. Revised November 27, 2019.
    c. Central Nervous System Cancers V3.2019. Revised October 18, 2019.
    d. Colon Cancer V1.2020. Revised December 19, 2019.
    e. Gestational Trophoblastic Neoplastic. V1.2020. Revised December 11, 2019.
    f. Head and Neck Cancer V3.2019. Revised September 16, 2019.
    g. Hepatobiliary Cancers V3.2019. Revised August 1, 2019
    h. Hodgkin Lymphoma V2.2019. Revised July 15, 2019.
    i. Kidney Cancer. V2.2020. Revised August 5, 2019.
    j. Malignant Pleural Mesothelioma V1.2020. Revised November 27, 2019.
    k. Cutaneous Melanoma V1.2020. Revised December 19, 2019
    l. Non-Small Cell Lung Cancer. V5.2020. Revised May 27, 2020.
    m. Rectal Cancer V1.2020. Revised December 19, 2019.
    n. Small Bowel Adenocarcinoma V1.2020. Revised July 30, 2019.
    o. Small Cell Lung Cancer. V2.2020. Revised November 15, 2019.
    p. Uveal Melanoma V1.2019. Revised June 14, 2019.
10. Overman MJ, Lonardi S, Wong KYM, et al. Durable clinical benefit with nivolumab plus ipilimumab in DNA mismatch repair-deficient/microsatellite instability-high metastatic colorectal cancer. *J Clin Oncol.* 2018;36:773-9. Available at: https://ascopubs.org/doi/pdf/10.1200/JCO.2017.76.9901.
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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.

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