Effective Date: 5/3/2018

Opdivo® (nivolumab)

FDA approval: 10/15/2014
HCPCS: J9299
Benefit: Medical

Policy/Criteria:

Note: Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided in patients 18 years or older who have not received prior treatment with a PD-1 inhibitor (example: Keytruda), when prescribed by an oncologist or a hematologist, and when all the below criteria are met:
   a. A diagnosis of unresectable or metastatic melanoma:
      1. As monotherapy
         OR
      2. In combination with Yervoy in patients with BRAF V600 wild-type. Requests for the combination therapy are evaluated by a clinician on a case by case basis and are determined following appropriate genetic testing and assessment of risks and benefits
   b. A diagnosis of metastatic non-small cell lung cancer:
      1. Documentation of disease progression on or after treatment with platinum-based chemotherapy
         AND
      2. If EGFR mutation positive, documentation of disease progression following treatment with EGFR inhibitor such as erlotinib (Tarceva) and afatinib (Gilotrif)
         AND
      3. If ALK mutation positive, documentation of disease progression following treatment with ALK inhibitor such as ceritinib (Zykadia)
         AND
      4. Use as monotherapy
   c. A diagnosis of RCC:
      1. Documentation of disease progression following treatment with at least one anti-angiogenic agent (examples: Sutent, Votrient, and Nexavar)
         AND
      2. Use as monotherapy
d. A diagnosis of classical Hodgkin lymphoma (cHL):
   1. Documentation of disease progression after autologous hematopoietic stem cell transplantation (HSCT) AND Adcetris (brentuximab vedotin) OR
   2. Documentation of disease progression after 3 or more lines of systemic therapy (such as ifosfamide with carboplatin and etoposide) that include autologous HSCT AND
   3. As monotherapy

e. A diagnosis of metastatic squamous cell carcinoma of the head and neck (SCCHN)
   1. Documentation of disease progression on or after treatment with platinum-based chemotherapy AND
   2. As monotherapy

f. A diagnosis of locally advanced or metastatic urothelial carcinoma (UC)
   1. Documentation of disease progression during or following platinum-containing chemotherapy OR
   2. Documentation of disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy AND
   3. Use as monotherapy

g. A diagnosis of metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer:
   1. ≥ 12 years old
   2. Documentation of disease progression following FOLFOXIRI (fluoropyrimidine, oxaliplatin, and irinotecan)

h. A diagnosis of hepatocellular carcinoma (HCC):
   1. Documentation of disease progression following sorafenib
   2. Use as monotherapy

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limit:
      i. Monotherapy: 3mg/kg every 2 weeks (limit 2 infusions/30 days)
      ii. Monotherapy: 240mg every 2 weeks
      iii. Combination therapy: 1mg/kg followed by Yervoy every 3 weeks for 4 doses. The recommended subsequent dose as a single agent is 3mg/kg every 2 weeks
   b. Initial Authorization Period: 6 months
   c. Renewal Criteria:
      1. No evidence of disease progression or unacceptable toxicity
   d. Renewal Authorization Period: 1 year

C. Opdivo is considered investigational when used for all other conditions, including but not limited to:
   a. In combination with other regimens for the treatment of NSCLC
   b. Breast cancer
   c. Metastatic castration-resistant prostate cancer
   d. Pancreatic cancer

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e. In combination with other regimens for the treatment of RCC
f. Other solid tumors

D. ***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Therapeutic Considerations:

A. FDA Approved Indication / Diagnoses
   1. Unresectable or metastatic melanoma:
      a. As a single agent.
      b. In combination with Yervoy
   2. Metastatic non-small cell lung cancer with progression on or after platinum-based chemotherapy. Patients with NSCLC and EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo
   3. Advanced renal cell carcinoma in patients who have received prior anti-angiogenic therapy
   4. Treatment of patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin or after 3 or more lines of systemic therapy that includes autologous HSCT
   5. Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy
   6. Locally advanced or metastatic urothelial carcinoma with disease progression during or following platinum-containing chemotherapy or disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

B. Background Information
   a. Metastatic melanoma:
      i. Melanoma is the 5th most common type of cancer in the United States. It forms in the body melanocyte cells, which develop the skin’s pigment. The National Cancer Institute estimates that 76,100 Americans will be diagnosed with the disease and 9,710 will die from melanoma this year.
      ii. Opdivo (nivolumab) is a monoclonal antibody (IgG4) directed against programmed death receptor-1 (PD-1). Opdivo binds to PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response. The binding and blocking of PD-1 activity enables T-cells and cytokines proliferation, allowing an anti-tumor immune response.
      iii. Opdivo is the 7th new melanoma drug approved by the FDA since 2011 and the 2nd in the class cleared by the FDA following the approval of Merck & Co.’s Keytruda® (pembrolizumab) in September 2014.
      iv. The scientific rationale for targeting the immune system via dual immune inhibition in cancer has formed the basis of a novel approach to the treatment of metastatic melanoma.
   b. NSCLC:
      i. Lung cancer is one of the leading causes of cancer deaths in the United States. NSCLC is one of the most common types of lung cancers and accounts for 85% of cases. Squamous NSCLC accounts for 25-30% of all lung cancers. Survival rates vary depending on the stage and type of cancer and when it is diagnosed.
      ii. Opdivo is the only PD-1 inhibitor approved for patients regardless of PD-L1 expression, and offers significant improvement over the current standard chemotherapy.
iii. Keytruda (the second PD-1 inhibitor) gained approval for the diagnosis of metastatic NSCLC with tumors that express PD-L1 as determined by an FDA-approved test with evidence of disease progression on or after platinum-containing chemotherapy.

iv. Opdivo expanded approval for NSCLC was granted by the FDA following an expedited review, making it the 1st immunotherapy approved for lung cancer and the second PD-1 inhibitor approved in the United States.

v. Opdivo is the only FDA approved monotherapy to demonstrate superior overall survival in patients with refractory NSCLC compared to standard therapies.

c. Clear-cell RCC:
   i. Renal cell carcinoma (RCC) is the most common type of kidney cancer in adults, accounting for more than 100,000 deaths worldwide each year. Clear-cell RCC is the most prevalent type of RCC and constitutes 80 percent to 90 percent of all cases.
   ii. RCC is approximately twice as common in men as in women, with the highest rates of the disease in North America and Europe. The five-year survival rate for those diagnosed with metastatic or advanced kidney cancer is 12.1 percent.
   iii. There are several types of renal cell cancer that include: clear cell, papillary, chromophobe, oncocytic, and collecting duct.
   iv. Opdivo was approved for the indication of RCC as the first immuno-oncology agent that has demonstrated a survival advantage in advanced renal cell carcinoma in patients that currently have limited treatment options.

d. (SCCHN):
   i. SCCHN accounts for more than 90% of all head and neck cancers, and more than 50% of SCCHN patients present with Stage III or higher disease (locally advanced or metastatic), which has higher potential for progression and recurrence.
   ii. The relative five-year survival rate for metastatic head and neck cancers is <38%, and can be as low as 4% for recurrent or metastatic Stage IV disease.
   iii. Opdivo is the first and only immuno-oncology treatment proven in a phase 3 trial to significantly extend overall survival in patients with recurrent or metastatic squamous cell head and neck cancer who had been previously treated with platinum-based therapy.

e. Urothelial carcinoma (UC)
   i. UC is the fifth most commonly diagnosed cancer in the United States, with an estimated 77,000 new diagnoses in 2016 and over 16,000 deaths. Urothelial carcinoma is the most common type of bladder cancer, accounting for approximately 90% of diagnoses. The majority of bladder cancers are diagnosed at an early stage, but rates of recurrence and progression are high and approximately 50-70% of patients will experience a recurrence within five years.
   ii. The poor durability of responses in the first-line setting presents a major challenge in the treatment of metastatic disease and there are limited treatment options in the second-line setting for advanced urothelial carcinoma.

f. Microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer
   i. refers to malignancies originating from the large intestine (colon) or the rectum. The term colorectal cancer does not include anal cancer. According to the American Cancer Society, there was an estimated 95,270 new cases of colon cancer and 39,220 new cases of rectal cancer diagnosed in 2016. In the US, colon cancer is the third leading type of cancer in males and the fourth in females. Risk factors for cancer of the colon and rectum (colorectal cancer) include colon polyps, long-standing ulcerative colitis, and genetic family history.

f. Hepatocellular carcinoma (HCC)
   i. The most common form of liver cancer with about 40,710 new cases of liver and intrahepatic bile duct cancer diagnosed in 2017 and nearly 28,920 deaths from the disease annually in the U.S. Chronic infections with hepatitis B virus (HBV) or hepatitis C virus are the most common cause of liver cancer.
C. Efficacy
  *Please refer to most recent prescribing information.

D. Medication Safety Considerations

Black Box Warning: No
*Please refer to most recent prescribing information.

E. Dosing and administration
  a. Dosing:
     i. 3mg/kg every 2 weeks (limit 2 infusions/30 days)
     ii. 240mg every 2 weeks (limit 2 infusions/30 days)
  *Please refer to most recent prescribing information.

F. How supplied
  a. 50mg vials

References:


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**Policy History**

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<td>Effective Date: 05/07/2015</td>
<td>New Criteria</td>
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<tr>
<td>1.1</td>
<td>Effective Date: 08/13/2015</td>
<td>Updated with a new indication of squamous non-small cell lung cancer</td>
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<td>1.2</td>
<td>Effective Date: 02/11/2016</td>
<td>Updated with a new indications of BRAF V600 wild-type metastatic melanoma and non-squamous NSCLC</td>
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<td>1.3</td>
<td>Effective Date: 05/05/2016</td>
<td>Updated with a new indications: as monotherapy in unresectable or metastatic melanoma in wild-type BRAF V600 and renal cell carcinoma</td>
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<td>1.4</td>
<td>Effective Date: 08/11/2016</td>
<td>Expanded indications: monotherapy and combination therapy with Yervoy in BRAF V600 mutation-Annual Review</td>
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<td>1.5</td>
<td>Effective Date: 11/10/2016</td>
<td>Expanded indication: classical Hodgkin lymphoma</td>
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|   | Effective Date: | Expanded indication: SCCHN  
Updated RCC to include non-clear cell  
Updated dosing for: melanoma, NSCLC, and RCC |
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*The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or [http://dailymed.nlm.nih.gov/dailymed/index.cfm](http://dailymed.nlm.nih.gov/dailymed/index.cfm)*