DESCRIPTION: Nivolumab is a human monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. Nivolumab is an IgG4 kappa immunoglobulin.

OPDIVO® (nivolumab) is indicated for the treatment of:

INDICATION(S):
- Patients with BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent
- Patients with BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent
- Patients with unresectable or metastatic melanoma, in combination with ipilimumab
- Patients with melanoma with lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting
- Patients with metastatic non-small cell lung cancer and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO
- Patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy
- Adult patients with classical Hodgkin lymphoma that has relapsed or progressed after
  - Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
  - 3 or more lines of systemic therapy that includes autologous HSCT
- Patients with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy
- Patients with locally advanced or metastatic urothelial carcinoma who:
  - Have disease progression during or following platinum-containing chemotherapy
  - Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
- Adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatched repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan
- Patients with hepatocellular carcinoma who have been previously treated with sorafenib

REASONS FOR PA:
- Cost
- Potential for misuse
- Toxicity
1. Patient is 12 years of age or greater for treatment for MSI-H or dMMR metastatic colorectal cancer, or an Adult, 18 years of age or greater for any other cancers; or

2. Patient is diagnosed with BRAF V600 wild-type unresectable or metastatic melanoma, and this drug will be used as a single agent; or

3. Patient is diagnosed with BRAF V600 mutation-positive unresectable or metastatic melanoma, and this drug will be used as a single agent; or

4. Patient is diagnosed with unresectable or metastatic melanoma, and this drug will be used in combination with ipilimumab; or

5. Patient is diagnosed with melanoma with lymph node involvement or metastatic disease who have undergone complete resection, and this drug will be used in the adjuvant setting; or

6. Patient is diagnosed with metastatic squamous non-small cell lung cancer (NSCLC) that progresses during or after treatment with platinum-based chemotherapy, and patients with EGFR or ALK genomic tumor aberrations with disease progression were on FDA-approved therapy for these aberrations prior to receiving OPDIVO; or

7. Patient is diagnosed with advanced renal cell carcinoma who have received prior antiangiogenic therapy; or

8. Patient is an adult with classical Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin; or

9. Patient is an adult with classical Hodgkin lymphoma that has relapsed or progressed after 3 or more lines of systemic therapy that includes autologous HSCT; or

10. Patient is diagnosed with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) that progresses during or after platinum-based therapy; or

11. Patient is diagnosed with locally advanced or metastatic urothelial carcinoma that progresses during or following platinum-containing chemotherapy; or

12. Patient is diagnosed with locally advanced or metastatic urothelial carcinoma that progresses within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; or

13. Patient is an adult or pediatric (12 years and older) with microsatellite instability-high (MSI-H) or mismatched repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan; or

14. Patient is diagnosed with hepatocellular carcinoma who has been previously treated with sorafenib; and

15. Patient is not currently showing signs of immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis and liver dysfunction, immune-mediated endocrinopathies, immune-mediated encephalitis, or immune-mediate myocarditis, rhabdomyolysis, myositis, uveitis, iritis, pancreatitis, facial and abducens nerve paresis, demyelination, polymyalgia rheumatica, autoimmune neuropathy, Guillain-Barre syndrome, hypopituitarism, systemic inflammatory response syndrome, gastritis, duodenitis, sarcoidosis, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), motor dysfunction, vasculitis, and myasthenic syndrome, or has a Serum Creatinine greater than 1.5 times the ULN; and

16. Patient has had a baseline liver function panel; and

17. Patient has had a baseline renal function panel; and

18. Patient has had a baseline thyroid function panel; and

19. Starting dose is 240 mg as an intravenous infusion over 30 minutes every 2 weeks OR OPDIVO with ipilimumab: OPDIVO 1 mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then OPDIVO 240 mg every 2 weeks or 480 mg every 4 weeks AND

20. Prescriber is an oncologist or is consulting with an oncologist

REASONS for DENIAL of BENEFIT:

1. Patient has hypersensitivity to OPDIVO® (nivolumab) or any of its components

2. Patient does not meet above criteria
RENEWAL CRITERIA:

1. Patient has demonstrated a response to therapy

BENEFIT APPROVAL:

Initial approval for a period of 3 months. Renewal approval period: 6 months

OPDIVO® (nivolumab) product package insert, Bristol-Myers Squibb Company, Princeton, NJ 08543 USA
March 2018

HISTORY

<table>
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<tr>
<th>Type of Revision</th>
<th>Summary of Changes</th>
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| Revised custom policy  | Updated new dosages 480 mg once every 4 weeks for most of its indications and a shorter infusion time (30 minutes) and a new size vial (240 mg) Updated indications and usage for:  
    • patients with melanoma with lymph node involvement or metastatic disease who have undergone complete resection, and drug will be used in the adjuvant setting  
    • patient with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy  
    • patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy, or disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy  
    • adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan  
    • patients with hepatocellular carcinoma who have been previously treated with sorafenib Corrected and updated approval criteria to change from patient not currently having SCr 1.5 mg/dl to SCr 1.5 times ULN and to include new warnings for immune-mediated hepatitis, other immune-mediated adverse reactions that require temporary or permanent drug discontinuation | 3/20/2018       |