I. Policy:
Opdivo (nivolumab)

II. Purpose/Objective:
To provide a policy of coverage regarding Opdivo (nivolumab)

III. Responsibility:
A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than
   the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

- appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
- provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;
- in accordance with current standards good medical treatment practiced by the general medical community;
- not primarily for the convenience of the Member, or the Member's Health Care Provider; and
- the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment
Medical Necessity shall mean a service or benefit that is compensable under the Medical Assistance Program and if it meets any one of the following standards:

(i) the service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.

(ii) the service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or development effects of an illness, condition, injury or disability.

(iii) the service or benefit will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for members of the same age.
**DESCRIPTION:**

Opdivo (nivolumab) is a fully human immunoglobulin G4 (IgG4) monoclonal antibody that selectively inhibits programmed cell death 1 (PD-1) activity by binding to the PD-1 receptor to block the ligands PD-L1 and PD-L2 from binding. The negative PD-1 receptor signaling that regulates T-cell activation and proliferation is therefore disrupted. This releases PD-1 pathway-mediated inhibition of the immune response, including the antitumor immune response.

**CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee**

**GRANDFATHER PROVISION** – Members already established on therapy are eligible for approval as long as there is medical record documentation that the safety and effectiveness of use for the prescribed indication is supported by Food and Drug Administration (FDA) approval or adequate medical and scientific evidence in the medical literature.

Opdivo (nivolumab) will be considered medically necessary when all of the following criteria are met:

1. **Melanoma**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - Medical record documentation of one of the following:
     - A diagnosis of unresectable or metastatic melanoma **AND**
     - Opdivo is not being used in combination with any other agents for the treatment of unresectable or metastatic melanoma (with the exception of ipilimumab).
     **OR**
     - A diagnosis of completely resected (no evidence of disease) metastatic melanoma with distant metastases, which may include lymph nodes **AND**
     - Medical record documentation of complete resection of distant metastases **AND**
     - Opdivo is being used in the adjuvant setting **AND**
     - Opdivo is being used as a single agent

   **(Note: The FDA-approved treatment duration for use of Opdivo in the adjuvant setting for completely resected metastatic melanoma is for up to 1 year, see specific reauthorization criteria below.)**

2. **Non-Small Cell Lung Cancer (NSCLC)**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - Medical record documentation of a diagnosis of metastatic non-small cell lung cancer (NSCLC) with disease progression while on or after platinum-based chemotherapy **AND**
   - Medical record documentation that Opdivo is not being used in combination with any other agents for the treatment of metastatic non-small cell lung cancer (NSCLC)

3. **Renal Cell Carcinoma**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - Medical record documentation of use as a single agent for relapse or for surgically unresectable advanced or metastatic renal cell carcinoma **AND**
   - Medical record documentation of a therapeutic failure on or intolerance to prior anti-angiogenic therapy, including, but not limited to, Sutent (sunitinib), Votrient ( pazopanib), Inlyta (axitinib), Nexavar (sorafenib), Avastin (bevacizumab), Afinitor (everolimus), or Torisel (temsirolimus).
   **OR**
   - Medical record documentation of previously untreated advanced renal cell carcinoma **AND**
   - Medical record documentation that the patient is at intermediate to poor risk (defined as having 1 or more 6 prognostic risk factors as per the IMDC criteria*) **AND**
   - Medical record documentation that Opdivo will be given in combination with ipilimumab (Yervoy)

*IMDC Criteria risk factors include:
1. Less than one year from time of initial renal cell carcinoma diagnosis to randomization
2. Karnofsky performance status <80%
3. Hemoglobin less than the lower limit of normal
4. Corrected calcium of greater than 10 mg/dL
5. Platelet count greater than the upper limit of normal
6. Absolute neutrophil count greater than the upper limit of normal
4. **Classical Hodgkin Lymphoma (CHL)**
   - Prescription written by a hematologist/oncologist AND
   - Medical record documentation that patient is ≥ 18 years of age AND
   - Medical record documentation of a diagnosis of classical Hodgkin lymphoma (CHL) that has relapsed or progressed after:
     - Autologous hematopoietic stem cell transplantation and post-transplantation brentuximab vedotin (Adcetris), OR
     - Three (3) or more lines of systemic therapy that includes autologous HSCT

5. **Squamous Cell Carcinoma of the Head and Neck (SCCHN)**
   - Prescription written by a hematologist/oncologist AND
   - Medical record documentation that patient is ≥ 18 years of age AND
   - Medical record documentation of a diagnosis of recurrent or metastatic squamous cell carcinoma of the head and neck AND
   - Medical record documentation of disease progression while on or after receiving a platinum-based therapy

6. **Urothelial Carcinoma**
   - Prescription written by a hematologist/oncologist AND
   - Medical record documentation that patient is ≥ 18 years of age AND
   - Medical record documentation of a diagnosis of locally advanced or metastatic urothelial carcinoma AND one of the following:
     - Disease progression during or following platinum-containing chemotherapy OR
     - Disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy AND
   - Medical record documentation that Opdivo is NOT being used in combination with any other agent

7. **Colorectal Cancer**
   - Prescription written by a hematologist/oncologist AND
   - Medical record documentation that patient is ≥ 12 years of age AND
   - Medical record documentation of a diagnosis of metastatic colorectal cancer AND
   - Medical record documentation of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease AND
   - Medical record documentation of progression following treatment with a fluoropyrimidine, oxaliplatin, or irinotecan AND
   - Medical record documentation that Opdivo is being used as a single agent or in combination with ipilimumab (Yervoy).

8. **Hepatocellular Carcinoma (HCC)**
   - Prescription written by a hematologist/oncologist AND
   - Medical record documentation of a diagnosis of hepatocellular carcinoma AND
   - Medical record documentation of a therapeutic failure on or intolerance to sorafenib (Nexavar)

9. **Small Cell Lung Cancer (SCLC)**
   - Prescription written by a hematologist/oncologist AND
   - Medical record documentation that patient is ≥ 18 years of age AND
   - Medical record documentation of a diagnosis of metastatic small cell lung cancer (SCLC) AND
   - Medical record documentation of disease progression after two different lines of therapy, one of which must be a platinum-based chemotherapy.
AUTHORIZATION DURATION:

**For adjuvant treatment of metastatic melanoma (completely resected melanoma):**
Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. One subsequent approval will be for an additional 6 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

Authorization of Opdivo for the adjuvant treatment of metastatic melanoma should not exceed the FDA-approved treatment duration of 1 year (12 months). For requests exceeding the above limit, medical record documentation of the following is required:
- Peer-reviewed literature citing well-designed clinical trials to indicate that the member’s healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

For all other indications:
Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

LINE OF BUSINESS:
Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy.

This policy will be revised as necessary and reviewed no less than annually.

Devised: 03/24/15

Revised: 5/19/15 (updated indication, NSCLC), 11/17/15 (updated criteria), 1/19/16 (updated indication, renal), 7/19/16 (updated indication CHL), 1/17/17 (SCCHN indication), 3/21/17 (urothelial indication), 5/8/17 (per DHS), 7/18/17 (updated CHL), 9/19/17 (colon cancer), 11/21/17 (hepatocellular), 3/20/18 (updated melanoma and auth duration), 4/24/18 (grandfather), 5/15/18 (untreated RCC), 9/18/18 (colorectal, SCLC)

Reviewed: 8/29/19