Geisinger

POLICIES AND PROCEDURE MANUAL

Policy: MBP 126.0

Section: Medical Benefit Pharmaceutical Policy

Subject: Opdivo (nivolumab)

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
3. the department requiring/authoring the policy.
4. Devised – the date the policy was implemented.
5. Revised – the date of every revision to the policy, including typographical and grammatical changes.
6. 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:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. 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
Medically Necessary — A service, item, procedure, or level of care compensable under the Medical Assistance program that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

i. Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
ii. Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
iii. 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 for all lines of business when all of the following criteria are met:

1. *Melanoma*
- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 12 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) Stage IIB, Stage IIC, Stage III, or Stage IV melanoma **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 stage IIB, stage IIC, stage III, and stage IV melanoma is for up to 1 year, see specific reauthorization criteria below.)*

2. *Non-Small Cell Lung Cancer (NSCLC)*

If the request is for metastatic NSCLC with progression after platinum-based chemotherapy:
- 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)

OR

If the request is for first-line treatment of metastatic NSCLC expressing PD-L1 (≥ 1%):
- Medical record documentation of a diagnosis of metastatic non-small cell lung cancer (NSCLC) **AND**
- Medical record documentation of PD-L1 ≥ 1% as determined by an FDA-approved test **AND**
- Medical record documentation of no EGFR or ALK genomic tumor aberrations **AND**
- Medical record documentation that Opdivo will be used for first-line treatment in combination with Yervoy

OR

If the request is for first-line treatment metastatic or recurrent NSCLC:
- Medical record documentation of a diagnosis of metastatic or recurrent non-small cell lung cancer (NSCLC) **AND**
- Medical record documentation of no EGFR or ALK genomic tumor aberrations **AND**
- Medical record documentation that Opdivo will be used for first-line treatment in combination with Yervoy and 2 cycles of platinum-doublet chemotherapy

OR

If the request is for neoadjuvant treatment of resectable NSCLC:
- Medical record documentation of resectable (tumor size greater than or equal to 4 centimeters or node-positive) non-small cell lung cancer (NSCLC) **AND**
- Medical record documentation that Opdivo will be used for neoadjuvant treatment in combination with platinum-doublet chemotherapy.

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** one of the following:
  o Medical record documentation that Opdivo will be given in combination with cabozantinib (Cabometyx)

OR

- 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 ≥ 18 years of age **AND**
- Medical record documentation of one of the following:
  - 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

  OR

  - Medical record documentation that Opdivo is being used in the adjuvant setting for a diagnosis of urothelial carcinoma AND both of the following:
    - Medical record documentation of radial resection of urothelial carcinoma AND
    - Medical record documentation of high risk of recurrence of urothelial carcinoma*

  AND

- Medical record documentation that Opdivo is NOT being used in combination with any other agent

**Note in clinical trials high risk of recurrence of urothelial carcinoma was defined as pathological stage of ypT2-ypT4a or ypN+ for patients who received neoadjuvant cisplatin or pathological stage of pT3-pT4a or pN+ for patients who did not receive neoadjuvant cisplatin due to ineligibility for or refusal of adjuvant cisplatin.*

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) **AND**
- Medical record documentation that Opdivo will be used as a single-agent or in combination with ipilimumab (Yervoy)

9. Esophageal Squamous Cell Carcinoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is 18 years of age or older **AND**
- One of the following:
    - Medical record documentation of unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC) **AND**
    - Medical record documentation of previous trial of fluoropyrimidine- and platinum-based chemotherapy.

  OR
    - Medical record documentation of unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) **AND**
    - Medical record documentation that Opdivo will be given in combination with fluoropyrimidine- and platinum-containing chemotherapy OR in combination with ipilimumab (Yervoy) **AND**
    - Medical record documentation that the regimen is being given as first-line treatment

10. Unresectable Malignant Pleural Mesothelioma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is 18 years of age or older **AND**
- Medical record documentation of unresectable malignant pleural mesothelioma **AND**
- Medical record documentation of use in combination with ipilimumab (Yervoy)

11. Adjuvant Treatment of Resected Esophageal or Gastroesophageal Junction Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease **AND**
- Medical record documentation that patient has received neoadjuvant chemoradiotherapy
- Medical record documentation Opdivo is being used in the adjuvant setting **AND**
- Medical record documentation Opdivo is being used as a single agent

(Note: The FDA-approved treatment duration for use of Opdivo in the adjuvant setting for resected esophageal or gastroesophageal junction cancer is for up to 1 year, see specific reauthorization criteria below.)

12. Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of advanced or metastatic gastric cancer, gastroesophageal junction cancer, or esophageal adenocarcinoma **AND**
- Medical record documentation that Opdivo will be used in combination with fluoropyrimidine- and platinum-based chemotherapy.

AUTHORIZATION DURATION:

****For adjuvant treatment of melanoma *(completely resected melanoma*), adjuvant treatment of resected esophageal or gastroesophageal junction cancer, and adjuvant urothelial carcinoma:**
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 melanoma, adjuvant treatment of resected esophageal or gastroesophageal junction cancer, or adjuvant treatment of urothelial carcinoma 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 first line-treatment of metastatic NSCLC expressing PD-L1 (≥ 1%), for first-line treatment of metastatic or recurrent NSCLC, and first line treatment of unresectable malignant pleural mesothelioma and treatment of gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma: Initial approval:**
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 **18 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 first line-treatment of metastatic NSCLC expressing PD-L1 (≥ 1%), for first-line treatment of metastatic or recurrent NSCLC, and first line treatment of unresectable malignant pleural mesothelioma and treatment of gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma: should not exceed the FDA-approved treatment duration of 2 years (24 months) in patients without disease progression. 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 Neoadjuvant NSCLC:** One approval will be given for up to **3 cycles for a total duration of 6 months**. Authorization of Opdivo for the neoadjuvant treatment of NSCLC should not exceed the FDA-approved treatment duration of 3 cycles. 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.

Note: For Medicaid (GHP Family), any requests for services that do not meet criteria set in the PARP will be evaluated on a case-by-case basis.

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.

REFERENCES:

1. Opdivo [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; October 2023.

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), 5/19/20 (HCC in combo with ipilimumab), 7/21/20 (NSCLC and ESCC), 11/17/20 (mesothelioma), 3/16/21 (updated RCC, removed SCLC), 6/18/21 (adjuvant esophageal/gastroesophageal indication, gastric/gastroesophageal/esophageal indications), 10/27/21 (adjuvant urothelial carcinoma), 5/17/22 (added neoadjuvant NSCLC & auth duration, added Medicaid PARP statement), 7/19/22 (first line ESCC), 4/25/23 (MM age, Medicare carve out, Medicaid business segment), 12/30/23 (references added), 1/2/24 (adjuvant treatment of melanoma edits from 12/2023)

Reviewed: 8/29/19

MA UM Committee approval: 12/31/23