## Prior Authorization Review Panel

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**CHC-MCO Policy Submission**

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

| | |
|---|---|
| **Plan: PA Health & Wellness** | **Submission Date: 02/01/2020** |
| **Policy Number: PA.CP.PHAR.121** | **Effective Date: 01/01/2018**<br>**Revision Date: 01/15/2020** |
| **Policy Name: Nivolumab (Opdivo)** | |

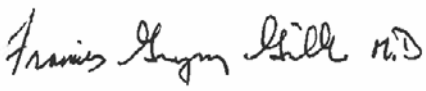
**Type of Submission – Check all that apply:**

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

**Please provide any changes or clarifying information for the policy below:**

**1Q 2020 annual review: added off-label use in malignant pleural mesothelioma per NCCN recommendation update from category 2B to category 2A; added requirement for use in anal carcinoma as second line or subsequent therapy; added requirement for use in gestational trophoblastic neoplasia following a platinum/etoposide-containing regimen or in methotrexate-resistant, high-risk disease; references reviewed and updated.**

| | |
|---|---|
| **Name of Authorized Individual (Please type or print):**<br><br>**Francis G. Grillo, MD** | **Signature of Authorized Individual:**<br>  |

# Clinical Policy: Nivolumab (Opdivo)

Reference Number: PA.CP.PHAR.121
Effective Date: 01/18
Last Review Date: 01/20

Coding Implications
Revision Log

**Description**
Nivolumab (Opdivo®) is a programmed death receptor-1 (PD-1) blocking antibody.

**FDA Approved Indication(s)**
Opdivo is indicated for the treatment of:

- 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 (NSCLC) and progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo.
- Patients with metastatic small cell lung cancer (SCLC) with progression after platinum based chemotherapy and at least one other line of therapy.
- Patients with advanced renal cell carcinoma (RCC) who have received prior antiangiogenic therapy.
- Patients with intermediate or poor risk, previously untreated advanced RCC, in combination with ipilimumab.
- Adult patients with classical [classic] Hodgkin lymphoma (CHL) 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 (SCCHN) with disease progression on or after a platinum-based therapy.
- Patients with locally advanced or metastatic urothelial carcinoma (UC) who:
  - have disease progression during or following platinum-containing chemotherapy or;
  - 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 mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, as a single agent or in combination with ipilimumab.
- Patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

**Policy/Criteria**
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Opdivo is **medically necessary** when one of the following criteria are met:

## I. Initial Approval Criteria

**A. Melanoma** (must meet all):

1. Diagnosis of melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a, b, or c):*
   a. Monotherapy: Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. In combination with Yervoy®: Dose does not exceed 1 mg/kg every 3 weeks for 4 doses, followed by 240 mg every 2 weeks or 480 mg every 4 weeks;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**B. Non-Small Cell Lung Cancer** (must meet all):

1. Diagnosis of metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has progressed on or after systemic therapy;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**C. Small Cell Lung Cancer** (must meet all):

1. Diagnosis of SCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Failure of platinum-containing regimen (e.g. cisplatin, carboplatin), unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 240 mg every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**D. Renal Cell Carcinoma** (must meet all):

1. Diagnosis of renal cell carcinoma (RCC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a, b, or c:*

a. Monotherapy: Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
b. In combination with Yervoy: Dose does not exceed 3 mg/kg every 3 weeks for 4 doses, followed by 240 mg every 2 weeks or 480 mg every 4 weeks;
c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**E. Classical Hodgkin Lymphoma** (must meet all):
1. Diagnosis of CHL;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has relapsed or progressed after autologous hematopoietic stem cell transplantation;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 240 mg every 2 weeks or 480mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**F. Squamous Cell Carcinoma of the Head and Neck** (must meet all):
1. Diagnosis of SCCHN;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has progressed on or after platinum-containing regimen (e.g., cisplatin, carboplatin);
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 240 mg every 2 weeks or 480mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**G. Urothelial Carcinoma** (must meet all):
1. Diagnosis of UC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Failure of a platinum-containing regimen (e.g., cisplatin, carboplatin), unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**H. Colorectal Cancer** (must meet all):
1. Diagnosis of unresectable or metastatic CRC;
2. Tumor is characterized as MSI-H or dMMR;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 12 years;
5. Dose does not exceed one of the following (a, b, or c):*
   a. Monotherapy: 240 mg every 2 weeks;
   b. In combination with Yervoy: 3 mg/kg every 3 weeks for 4 doses, then 240 mg every 2 weeks;
   *c.* Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**I. Hepatocellular Carcinoma** (must meet all):
1. Diagnosis of HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member has had disease progression following treatment with Nexavar®;
   **Prior authorization may be required for Nexavar.*
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**J. Off-label NCCN Compendium Recommended Indications** (must meet all)**:**
1. Diagnosis of one of the following (a, b, c, or d):
   a. Metastatic squamous cell anal carcinoma;
   b. Metastatic Merkel cell carcinoma;
   c. Gestational trophoblastic neoplasia;
   d. Malignant pleural mesothelioma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For anal carcinoma: Prescribed as second line or subsequent therapy (examples of prior therapy include 5-FU/cisplatin, carboplatin/paclitaxel, FOLFOX, FOLFCIS);
5. For gestational trophoblastic neoplasia, prescribed as one of the following (a or b):
   a. Following treatment with a platinum/etoposide-containing regimen;
   b. Disease is methotrexate-resistant and high-risk (*see appendix D*);
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**K. Other diagnoses/indications:** Refer to PA.CP.PHAR.53

## II. Continued Approval

**A. All Indications in Section I** (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;*
3. If request is for a dose increase, request meets one of the following (a or b):*
    a. New dose does not exceed 480 mg every 4 weeks;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 12 months**

**B. Other diagnoses/indications** (1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;

**Approval duration: Duration of request or 6 months (whichever is less);** or

2. Refer to PA.CP.PHAR.53

## III. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

ALK: anaplastic lymphoma kinase
BRAF: B-Raf proto-oncogene, serine/threonine kinase
CHL: classic Hodgkin lymphoma
CRC: colorectal cancer
dMMR: mismatch repair deficient
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
HCC: hepatocellular carcinoma
HSCT: hematopoietic stem cell transplantation
MSI-H: microsatellite instability-high
NSCLC: non-small cell lung cancer
PD-1: programmed death receptor-1
RCC: renal cell carcinoma
SCLC: small cell lung cancer
UC: urothelial carcinoma

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Nexavar (sorafenib) | HCC: 400 mg PO BID until clinical benefit cease sor unacceptable toxicity occurs | 800 mg/day |
| Cisplatin- or carboplatin-containing chemotherapy | SCLC, UC, SCCHN: Varies | Varies |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| First-line therapies for metastatic anal carcinoma (e.g., 5-FU/cisplatin, carboplatin/paclitaxel, FOLFOX, FOLFCIS) | Varies | Varies |
| First-line therapies for gestational trophoblastic neoplasia (e.g., platinum/etoposide-containing regimen) | Varies | Varies |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*
None reported

*Appendix D: General Information*

- High-risk disease in gestational trophoblastic neoplasia is defined as having a FIGO stage II to III and ≥ 7 prognostic score or stage IV
  - FIGO staging system:

| Stage | Criteria |
|---|---|
| I | Tumor confined to uterus |
| II | Tumor extends to other genital structures (ovary, tube, vagina, broad ligaments) by metastasis or direct extension |
| III | Lung metastasis |
| IV | All other distant metastases |

  - Prognostic Scoring Index
    - The total score is obtained by adding the individual scores for each prognostic factor (low risk is indicated by a score < 7 and high risk is indicated by a score ≥ 7)

| Prognostic factor | Risk score | | | |
|---|---|---|---|---|
| | 0 | 1 | 2 | 4 |
| Age (years) | < 40 | ≥ 40 | -- | -- |
| Antecedent pregnancy | Hydatidiform mole | Abortion | Term pregnancy | -- |
| Interval from index pregnancy (months) | < 4 | 4 to 6 | 7 to 12 | >12 |
| Pretreatment hCG (IU/L) | $< 10^3$ | $10^3$ to $< 10^4$ | $10^4$ to $10^5$ | $\geq 10^5$ |

| | | | | |
|---|---|---|---|---|
| Largest tumor size, including uterus (cm) | < 3 | 3 to 5 | > 5 | |
| Site of metastases | Lung | Spleen, kidney | Gastrointestinal tract | Brain, liver |
| Number of metastases identified | 0 | 1 to 4 | 5 to 8 | > 8 |
| Previous failed chemotherapy | -- | -- | Single drug | Two or more drugs |
| Total score | -- | -- | -- | -- |

## IV. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Melanoma - unresectable or metastatic | Monotherapy: 240 mg IV every 2 weeks or 480 mg IV every 4 weeks<br><br>With ipilimumab: 1 mg/kg IV, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks | 480 mg/dose |
| Melanoma - adjuvant treatment<br>NSCLC<br>RCC - advanced with previous anti-angiogenic therapy<br>CHL, SCCHN, UC, HCC | 240 mg IV every 2 weeks or 480 mg IV every 4 weeks | 480 mg/dose |
| MSI-H or dMMR CRC | Monotherapy: 240 mg IV every 2 weeks<br><br>With ipilimumab: 3 mg/kg IV, followed by ipilimumab 1 mg/kg on the same day every 3 weeks for 4 doses, then nivolumab 240 mg IV every 2 weeks | Monotherapy: 240 mg/dose<br><br>With ipilimumab: 3 mg/kg/dose |
| RCC - advanced previously untreated | Monotherapy: 240 mg IV every 2 weeks or 480 me every 4 weeks<br><br>With ipilimumab: 3 mg/kg IV, followed by ipilimumab 1 mg/kg IV on the same day every 3 weeks for 4 doses, then nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks | 480 mg/dose |

## V. Product Availability

Single-dose vials: 40 mg/4 mL, 100 mg/10 mL, 240 mg/24 mL

## VI. References

1. Opdivo Prescribing Information. Princeton, NJ: Bristol-Myers Squibb; September 2019. Available at https://www.opdivo.com/. Accessed November 22, 2019.
2. Bavencio Prescribing Information. Rockland, MD: EMD Serono, Inc.; October 2017. Available at https://www.emdserono.com/content/dam/web/corporate/non-images/country-specifics/us/pi/bavencio-pi.pdf. Accessed September 26, 2018.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at http://www.nccn.org. Accessed November 22, 2019.

### Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| J9299 | Injection, nivolumab, 1 mg |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| Added requirement for being prescribed by or in consultation with an oncologist; added requirement for Child-Pugh classification to for HCC indication; updated melanoma criteria set to reflect expanded indication for the adjuvant treatment of patients with melanoma: removed "unresectable or metastatic" from the diagnosis. Added coverage criteria for the new FDA-approved indication of hepatocellular carcinoma. Updated off-label usage requirements for NSCLC, RCC, Classical Hodgkin lymphoma, squamous cell carcinoma of the head and neck and urothelial carcinoma to reflect off-label NCCN recommendations for use. Added coverage criteria for the new FDA-approved indication of MSI-H/dMMR colorectal cancer and for the NCCN-recommended off-label usages of malignant pleural mesothelioma and small cell lung cancer. References reviewed and updated. | 02/18 | |
| 1Q 2019 annual review; ages adjusted per PI to 18 and older for all indications except CRC; melanoma - brain metastasis is deleted and incorporated under a diagnosis of melanoma; for NSCLC, progression on platinum therapy changed to progression on systemic therapy to encompass progression on first-line targeted therapy per PI and NCCN; removed malignant pleural mesothelioma due to NCCN 2B recommendation status; off-label NCCN recommended trophoblastic tumor is added; dMMR/MSI-H metastatic rectal cancer removed from off-label section as it is represented under the CRC labeled use; for RCC, combination dosing with Yervoy added per PI; references reviewed and updated. | 01/19 | |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| 1Q 2020 annual review: added off-label use in malignant pleural mesothelioma per NCCN recommendation update from category 2B to category 2A; added requirement for use in anal carcinoma as second line or subsequent therapy; added requirement for use in gestational trophoblastic neoplasia following a platinum/etoposide-containing regimen or in methotrexate-resistant, high-risk disease; references reviewed and updated. | 01/20 | |