Opdivo

Description

Opdivo (nivolumab)

Background
Opdivo is a monoclonal antibody for the treatment of patients with unresectable (cannot be removed by surgery), metastatic (advanced) melanoma, adjuvant treatment of melanoma and metastatic non-small cell lung cancer, metastatic small cell lung cancer, renal cell carcinoma, hepatocellular carcinoma, relapsed or progressed classical Hodgkin lymphoma, recurrent or metastatic squamous cell carcinoma of the head and neck, locally advanced or metastatic urothelial carcinoma, or microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer who are no longer responding to other drugs. Opdivo works by inhibiting the PD-1 protein on cell surfaces, which blocks the immune system from attacking melanoma tumors (1).

Regulatory Status
FDA-approved indication: Opdivo is a human programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of patients with: (1)

1. Unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab

2. Adjuvant Treatment of Melanoma
   a. Melanoma with lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting

3. Metastatic non-small cell lung cancer with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have
disease progression on a FDA-approved therapy for these aberrations prior to receiving Opdivo

4. Metastatic small cell lung cancer with progression after platinum-based chemotherapy and at least one other line of therapy

5. Advanced renal cell carcinoma in patients who have received prior anti-angiogenic therapy

6. Intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with ipilimumab

7. Classical Hodgkin lymphoma that has relapsed or progressed after:
   a. Autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin, OR
   b. 3 or more lines systemic therapy that includes autologous HSCT

8. Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy

9. Locally advanced or metastatic urothelial carcinoma who:
   a. Have disease progression during or following platinum-containing chemotherapy
   b. Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

10. Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, as a single agent or in combination with ipilimumab (Yervoy)

11. Hepatocellular carcinoma that has been previously treated with sorafenib (Nexavar)

**Off-Label Uses:** (2)

1. Malignant pleural mesothelioma
2. Small cell lung cancer
3. Metastatic anal cancer
4. Merkel cell carcinoma

Clinically significant immune-mediated adverse reactions may occur with Opdivo therapy including pneumonitis, colitis, hepatitis, nephritis, renal dysfunction, hyperthyroidism, and
hypothyroidism. Patients should be monitored for signs and symptoms of adverse reactions and based on the severity, Opdivo should be withheld or discontinued and corticosteroids administered. Opdivo may cause fetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised of the potential hazard to a fetus. Opdivo is administered every 2 weeks until disease progression or unacceptable toxicity (1).

The safety and effectiveness of Opdivo have been established in pediatric patients age 12 years and older (1).

**Related Policies**

Bavencio, Imfinzi, Keytruda, Tecentriq, Yervoy

**Policy**

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Opdivo may be considered **medically necessary** in patients 12 years of age or older for unresectable or metastatic melanoma, adjuvant treatment of melanoma, metastatic non-small cell lung cancer, metastatic small cell lung cancer, renal cell carcinoma, relapsed or progressed classical Hodgkin lymphoma, recurrent or metastatic squamous cell carcinoma, locally advanced or metastatic urothelial carcinoma, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, hepatocellular carcinoma, malignant pleural mesothelioma, small cell lung cancer, metastatic anal carcinoma, or Merkel cell carcinoma; and if the conditions indicated below are met.

Opdivo is considered **investigational** in all other patients and for all other indications.

**Prior-Approval Requirements**

**Age**

12 years of age and older

**Diagnoses**

Patient must have **ONE** of the following:

1. Unresectable or metastatic melanoma
   a. Used as a single agent **OR** in combination with ipilimumab (Yervoy)
2. Adjuvant treatment of melanoma post resection

3. Metastatic non-small cell lung cancer with **ONE** of the following:
   a. Disease must have progressed while on or after platinum-based chemotherapy
   b. If EGFR or ALK genomic tumor aberration, had disease progression on FDA approved therapy

4. Metastatic small cell lung cancer
   a. Progression after platinum-based chemotherapy
   b. Progression after at least one other line of therapy

5. Advanced renal cell carcinoma with **ONE** of the following:
   a. Prior treatment with anti-angiogenic therapy
   b. Patient is considered to have an intermediate or poor prognosis
      i. Used in combination with ipilimumab (Yervoy)

6. Relapsed or progressed classical Hodgkin lymphoma with **ONE** of the following:
   a. Patient has had autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation therapy with brentuximab vedotin (Adcetris)
   b. Patient has had 3 or more lines systemic therapy that includes autologous HSCT

7. Recurrent or metastatic squamous cell carcinoma of the head and neck
   a. Disease must have progressed while on or after platinum-based chemotherapy

8. Locally advanced or metastatic urothelial carcinoma with **ONE** of the following:
   a. Disease must have progressed while on or after platinum-based chemotherapy
   b. Disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

9. Hepatocellular carcinoma
   a. Prior treatment with sorafenib (Nexavar)

10. Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer
a. Progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan
b. Diagnosis has to be confirmed by PCR-based assay genetic testing
c. Used as a single agent OR in combination with ipilimumab (Yervoy)

11. Malignant pleural mesothelioma
12. Small cell lung cancer
13. Metastatic anal carcinoma
14. Merkel cell carcinoma

Prior – Approval Renewal Requirements

Age 12 years of age and older

Diagnoses

Patient must have ONE of the following:

1. Unresectable or metastatic melanoma
2. Adjuvant treatment of melanoma post resection
3. Metastatic non-small cell lung cancer
4. Metastatic small cell lung cancer
5. Advanced renal cell carcinoma
6. Relapsed or progressed classical Hodgkin lymphoma
7. Recurrent or metastatic squamous cell carcinoma of the head and neck
8. Locally advanced or metastatic urothelial carcinoma
9. Hepatocellular carcinoma
10. Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer
11. Malignant pleural mesothelioma
12. Small cell lung cancer
13. Metastatic anal carcinoma
14. Merkel cell carcinoma

AND the following for ALL indications:
Prescriber agrees to discontinue treatment for any immune mediated adverse reaction (encephalitis, nephritis, rash, decreased renal function and endocrinopathies) or disease progression.

### Policy Guidelines

#### Pre - PA Allowance
None

#### Prior - Approval Limits

**Duration**  
6 months

#### Prior – Approval *Renewal* Limits

**Duration**  
12 months

### Rationale

**Summary**

Opdivo is a monoclonal antibody indicated for the treatment of various types of cancers. Opdivo works by inhibiting the PD-1 protein on cell surfaces, which blocks the immune system from attacking melanoma tumors. Opdivo may cause fetal harm when administered to a pregnant woman (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Opdivo while maintaining optimal therapeutic outcomes.

### References


### Policy History

<table>
<thead>
<tr>
<th>Date</th>
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<tbody>
<tr>
<td>January 2015</td>
<td>Addition to PA</td>
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<tr>
<td>March 2015</td>
<td>Annual editorial review and reference update</td>
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<td>Addition of Metastatic squamous non-small cell lung cancer</td>
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June 2015  Annual review
October 2015 Addition of BRAF V600 wild-type, the patient must use in combination with ipilimumab, and metastatic non-small cell lung cancer with the squamous cell requirement along with disease must have progressed after FDA-approved therapy if patient has EGFR or ALK tumor expression option.
December 2015 Annual review
Addition of new indication of renal cell carcinoma after prior treatment with an anti-angiogenic therapy
March 2016 Annual review
Removal of requirements: disease progression following Yervoy (ipilimumab) if BRAF V600 mutation positive, a BRAF inhibitor, BRAF V600 wild-type the patient must use in combination with ipilimumab
Policy number change from 5.04.53 to 5.21.53
June 2016 Annual review
Addition of relapsed or progressed classical Hodgkin lymphoma in patients who have had autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation therapy with brentuximab vedotin (Adcetris).
Addition of Prescriber agrees to discontinue treatment for any immune mediated adverse reaction (encephalitis, nephritis, rash, decreased renal function and endocrinopathies) or disease progression in renewal section per SME
September 2016 Annual review
December 2016 Addition of recurrent or metastatic squamous cell carcinoma of the head and neck with progression on or after platinum-based chemotherapy
February 2017 Addition of locally advanced or metastatic urothelial carcinoma with 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
June 2017 Annual editorial review
Addition to the relapsed or progressed classical Hodgkin lymphoma: patient has had 3 or more lines systemic therapy that includes autologous HSCT
August 2017 Addition of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer
September 2017 Annual review
October 2017 Addition of hepatocellular carcinoma
December 2017 Annual review
January 2018 Addition of melanoma with lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting
March 2018 Annual review
<table>
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<tr>
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<tr>
<td>May 2018</td>
<td>Addition of indication: Intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with ipilimumab; malignant pleural mesothelioma, small cell lung cancer, metastatic anal carcinoma, and Merkel cell carcinoma; and changed the age from 18 to 12 yrs of age</td>
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<tr>
<td>June 2018</td>
<td>Annual review</td>
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<tr>
<td>July 2018</td>
<td>Addition of indication: metastatic colorectal cancer as a single agent or in combination with ipilimumab</td>
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<tr>
<td>August 2018</td>
<td>Addition of metastatic small cell lung cancer, progression after platinum-based chemotherapy and at least one other line of therapy</td>
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<tr>
<td>September 2018</td>
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<tr>
<td>November 2018</td>
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<tr>
<td>March 2019</td>
<td>Change to indication: unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab</td>
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**Keywords**

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.