

## UTILIZATION REVIEW MEDICAL POLICY

**POLICY:** Oncology (Injectable) – Opdivo Utilization Review Medical Policy

- Opdivo® (nivolumab injection for intravenous use – Bristol-Myers Squibb)

**REVIEW DATE:** 12/18/2019; selected revision 06/24/2020

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### OVERVIEW

Opdivo, a human programmed death receptor-1 (PD-1) blocking antibody, is indicated for the treatment of the following:<sup>1</sup>

- **Classical Hodgkin lymphoma**, for adults that have relapsed or progressed after\*\* autologous hematopoietic stem cell transplantation (auto-HSCT) and Adcetris® (brentuximab vedotin intravenous injection) OR three or more lines of systemic therapy that includes auto-HSCT.
- **Colorectal cancer**, with or without Yervoy for patients ≥ 12 years of age with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic disease that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.\*\*
- **Esophageal squamous cell carcinoma**, for patients with unresectable advanced, recurrent, or metastatic disease after prior fluoropyrimidine- and platinum-based chemotherapy.
- **Head and neck squamous cell carcinoma**, in patients with recurrent or metastatic disease with disease progression on or after platinum-based therapy.
- **Hepatocellular carcinoma**, in patients who have been previously treated with Nexavar® (sorafenib tablets), with or without Yervoy.\*\*
- **Melanoma**, in patients with:
  - Unresectable or metastatic disease as a single agent, OR
  - Unresectable or metastatic disease in combination with Yervoy® (ipilimumab intravenous injection) in patients with melanoma;\* AND
  - Lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting.
- **Non-small cell lung cancer:**
  - As first-line treatment in combination with Yervoy, in adults with metastatic disease expressing programmed death-ligand 1 (≥ 1%) as determined by an FDA-approved test, without epidermal growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations; AND
  - As first-line treatment in combination with Yervoy and two cycles of platinum-doublet chemotherapy, in adults with recurrent or metastatic disease without *EGFR* or *ALK* genomic tumor aberrations; AND
  - In patients with metastatic disease 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.
- **Renal cell carcinoma (RCC):**
  - In patients with advanced disease who have received prior anti-angiogenic therapy; AND
  - In combination with Yervoy, for patients with intermediate or poor risk and previously untreated advanced RCC.
- **Small cell lung cancer**, in patients with metastatic disease with progression after platinum-based chemotherapy and at least one other line of therapy.\*\*
- **Urothelial carcinoma**, in patients with advanced or metastatic disease 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.

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\* This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

\*\* This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

### **POLICY STATEMENT**

Prior authorization is recommended for medical benefit coverage of Opdivo. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Opdivo as well as the monitoring required for adverse events and long-term efficacy, approval requires Opdivo to be prescribed by or in consultation with a physician who specializes in the condition being treated.

### **RECOMMENDED AUTHORIZATION CRITERIA**

Coverage of Opdivo is recommended in those who meet one of the following criteria:

#### **FDA-Approved Indications**

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**1. Classic Hodgkin Lymphoma (cHL).** Approve for 1 year if the patient meets BOTH of the following (A and B):

A) ONE the following conditions applies (i, ii, or iii):

- i. Patient has had a hematopoietic stem cell transplantation (HSCT); OR
- ii. Patient has tried three or more systemic regimens AND this includes an auto-HSCT as one line of therapy; OR

Note: Examples are ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine), Sanford V (doxorubicin, vinblastine, mechlorethamine, etoposide, vincristine, bleomycin, and prednisone), escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone).

- iii. Patient is not eligible for transplant according to the prescriber; AND

B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A or B):

- A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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**2. Colon or Rectal Cancer, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):

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- A) Patient is  $\geq 12$  years of age; AND
- B) One of the following applies (i or ii):
  - i. Patient has tried chemotherapy; OR  
Note: Examples of chemotherapy are fluoropyrimidine such as 5-fluorouracil (5-FU), capecitabine; oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin).
  - ii. Patient has unresectable or metastatic disease and is not a candidate for intensive therapy, according to the prescriber; AND
- C) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A, B, or C):

- A) 240 mg administered as an intravenous infusion not more frequently than once every 2 weeks; OR
- B) 480 mg administered as an intravenous infusion not more frequently than once every 4 weeks; OR
- C) Up to 3 mg/kg administered as an intravenous infusion not more frequently than once every 2 weeks.

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**3. Esophageal Squamous Cell Carcinoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient has tried fluoropyrimidine- and platinum-based chemotherapy; AND  
Note: Examples of fluoropyrimidines are 5-fluorouracil (5-FU) and capecitabine. Examples of platinum medications are cisplatin, carboplatin, and oxaliplatin.
- B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A or B):

- A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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**4. Head and Neck Squamous Cell Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):

- A) Patient has non-nasopharyngeal disease; AND
- B) Patient meets ONE of the following conditions (i or ii):
  - i. Patient has tried chemotherapy; OR  
Note: Examples of chemotherapy are cisplatin, carboplatin, Erbitux<sup>®</sup> (cetuximab intravenous infusion), 5-fluorouracil (5-FU), capecitabine, paclitaxel, docetaxel, methotrexate (MTX).
  - ii. A platinum-containing chemotherapy regimen or other chemotherapy is contraindicated, according to the prescriber; AND
- C) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A or B):

- A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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**5. Hepatocellular Carcinoma, Including Hepatobiliary Cancers.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient has tried at least one tyrosine kinase inhibitor (TKI) [e.g., Nexavar {sorafenib tablets}, Lenvima {levatinib capsules}]; AND

B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A, B, or C):

- A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
- C) 1 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

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6. **Melanoma** [Note: This includes cutaneous melanoma, brain metastases due to melanoma, and uveal melanoma]. Approve for the duration noted if the patient meets BOTH of the following (A and B):

- A) Patient meets ONE of the following (i or ii):
  - i. Approve for 1 year if the patient has unresectable, advanced, or metastatic melanoma; OR
  - ii. Approve for up to 1 year of treatment (total) if Opdivo will be used as adjuvant treatment (e.g., in a patient with no evidence of disease following resection of node-positive disease, locoregional recurrence, or in-transit recurrence); AND
- B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A, B, or C):

- A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
- C) Up to 1 mg per kg as an intravenous infusion administered not more frequently than once every 3 weeks.

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7. **Non-Small Cell Lung Cancer (NSCLC).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):

- A) The medication is prescribed by or in consultation with an oncologist; AND
- B) Patient has advanced or metastatic disease; AND
- C) Patient meets one of the following (i or ii):
  - i. Opdivo is used as first-line therapy and the patient meets all of the following (a, b, and c):
    - a) Patient's tumor expresses programmed death-ligand 1 (PD-L1)  $\geq 1\%$  as determined by an FDA-approved test; AND
    - b) Opdivo will be used in combination with Yervoy<sup>®</sup> (ipilimumab intravenous injection); AND
    - c) Patient's tumor is negative for a targetable mutation; OR  
Note: Examples of targetable mutations include sensitizing epidermal growth factor receptor (*EGFR*) mutation, anaplastic lymphoma kinase (*ALK*) fusions, *ROS1*, *BRAF*, *MET* *14* skipping mutation, *RET* rearrangement.
  - ii. Opdivo is used as subsequent therapy and the patient meets all of the following (a, b, and c):
    - a) Patient has tried systemic chemotherapy; AND  
Note: Examples of systemic chemotherapy include cisplatin, carboplatin, Alimta (pemetrexed injection), Abraxane (paclitaxel albumin-bound injection), gemcitabine, paclitaxel.
    - b) Patient has not progressed on prior therapy with a programmed death-1 (PD-1)/PD-ligand 1 (PD-L1) inhibitor; AND  
Note: This includes previous therapy with either one of Opdivo, Keytruda (pembrolizumab for injection), or Tecentriq (atezolizumab for injection).

- c) If non-squamous cell carcinoma (that is, adenocarcinoma, large cell, or NSCLC not otherwise specified) AND the patient's tumor is positive for a targetable mutation, the patient has received targeted drug therapy for the specific mutation.

Note: Examples of targetable mutations include sensitizing epidermal growth factor receptor (*EGFR*) mutation, anaplastic lymphoma kinase (*ALK*) fusions, *ROS1*, *BRAF*, *MET* *14* skipping mutation, *RET* rearrangement.

**Dosing.** Approve the following dosing regimens (A, B, C, or D):

- A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- B) 360 mg as an intravenous infusion administered not more frequently than once every 3 weeks; OR
- C) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
- D) Up to 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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**8. Renal Cell Carcinoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient has advanced (e.g., relapsed, Stage IV, or metastatic) disease; AND
- B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A, B, or C):

- A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR
- C) Up to 3 mg per kg as an intravenous infusion administered not more frequently than once every 3 weeks.

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**9. Small Cell Lung Cancer.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient has tried at least one other chemotherapy regimen; AND

Note: Examples of chemotherapy are cisplatin, carboplatin, etoposide, irinotecan, topotecan, paclitaxel.

- B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A, B, or C):

- A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- B) Up to 3 mg/kg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- C) Up to 3 mg/kg as an intravenous infusion administered not more frequently than once every 4 weeks.

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**10. Urothelial Carcinoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient has tried at least one other chemotherapy regimen; AND

Note: Examples of chemotherapy regimens are cisplatin, carboplatin, gemcitabine, Keytruda (pembrolizumab intravenous infusion), Tecentriq (atezolizumab intravenous infusion).

- B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A or B):

- A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR
- B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

### Other Uses With Supportive Evidence

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**11. Anal Carcinoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

A) Patient has received other chemotherapy; AND

Note: Examples of chemotherapy are 5-fluorouracil (5-FU), cisplatin, carboplatin plus paclitaxel, FOLFOX (oxaliplatin, leucovorin, and 5-FU).

B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A or B):

A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR

B) 3 mg per kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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**12. Extranodal NK/T-Cell Lymphoma, Nasal Type.** Approve for 1 year if the patient meets the following criteria (A and B):

A) Patient has received an asparaginase-based chemotherapy regimen.

Note: Examples of asparaginase-based chemotherapy are dexamethasone, ifosfamide, pegaspargase, etoposide; and gemcitabine, pegaspargase, oxaliplatin; AND

B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A or B):

A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR

B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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**13. Gestational Trophoblastic Neoplasia.** Approve for 1 year if the patient meets both of the following (A and B):

A) Patient meets one of the following (i or ii):

i. Patient has tried at least one previous chemotherapy regimen for recurrent or progressive disease; OR

Note: Examples of chemotherapy regimens contain etoposide, cisplatin/carboplatin, paclitaxel, bleomycin, ifosfamide, methotrexate.

ii. Patient has methotrexate-resistant high-risk disease; AND

B) The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A or B):

A) 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR

B) 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks.

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**14. Malignant Pleural Mesothelioma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

A) Patient has tried first-line chemotherapy; AND

Note: Examples of chemotherapy are Alimta (pemetrexed intravenous injection) plus cisplatin or carboplatin, Alimta with cisplatin and bevacizumab, gemcitabine plus cisplatin, Alimta alone, vinorelbine.

**B)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve up to 3 mg per kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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**15. Merkel Cell Carcinoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

**A)** Patient has disseminated Merkel cell carcinoma; AND

**B)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve 3 mg per kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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**16. Small Bowel Adenocarcinoma.** Approve for 1 year if the patient meets the following criteria (A, B, and C):

**A)** Patient has advanced or metastatic disease that is deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H); AND

**B)** Patient meets one of the following criteria (i or ii):

**i.** If the medication is used as initial therapy, the patient has tried oxaliplatin in the adjuvant setting or has a contraindication to oxaliplatin; OR

**ii.** The medication will be used as subsequent therapy; AND

**C)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimens (A, B, or C):

**A)** 240 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR

**B)** 480 mg as an intravenous infusion administered not more frequently than once every 4 weeks; OR

**C)** 3 mg per kg as an intravenous infusion administered not more frequently than once every 2 weeks.

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#### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Opdivo is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

#### REFERENCES

1. Opdivo® injection [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; June 2020.
2. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (Version 2.2019 – July 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
3. The NCCN Drugs & Biologics Compendium. © 2020 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 8, 2020. Search term: nivolumab.
4. The NCCN Head and Neck Cancers Clinical Practice Guidelines in Oncology (Version 3.2019 – September 16, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
5. The NCCN Hepatobiliary Cancer Clinical Practice Guidelines in Oncology (Version 3.2019 – August 1, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
6. The NCCN Melanoma Clinical Practice Guidelines in Oncology (Version 3.2019 – October 22, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
7. The NCCN Uveal Melanoma Clinical Practice Guidelines in Oncology (Version 1.2019 – June 14, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 8, 2019.

8. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (Version 4.2019 – November 8, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
9. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (Version 3.2019 – September 26, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
10. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 5.2020 – May 27, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 8, 2020.
11. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (Version 2.2020 – August 5, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
12. The NCCN Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 2.2020 – November 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
13. The NCCN Bladder Cancer Clinical Practice Guidelines in Oncology (Version 1.2020 – November 27, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
14. The NCCN Anal Carcinoma Clinical Practice Guidelines in Oncology (Version 1.2020 – November 19, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
15. The NCCN Gestational Trophoblastic Neoplasia Cancer Clinical Practice Guidelines in Oncology (Version 1.2020 – December 11, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 11, 2019.
16. The NCCN Malignant Pleural Mesothelioma Clinical Practice Guidelines in Oncology (Version 1.2020 – November 27, 2019) © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
17. The NCCN Merkel Cell Carcinoma Clinical Practice Guidelines in Oncology (Version 1.2020 – October 2, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
18. The NCCN Small Bowel Adenocarcinoma Clinical Practice Guidelines in Oncology (Version 1.2020 – July 30, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on December 17, 2019.
19. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 1.2020 – January 6, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 8, 2020.

## HISTORY

Type of Revision	Summary of Changes	Review Date
Selected Revision	New indication added for urothelial carcinoma	02/22/2017
Selected Revision	Revised cHL and urothelial carcinoma criteria.	06/14/2017
Selected Revision	Revised cHL to remove Deauville score is 4 or 5.	06/28/2017



Annual Revision	<ul style="list-style-type: none"> <li>• cHL: added that the dosing is in patients <math>\geq 18</math> years of age and is for Opdivo used as a single agent.</li> <li>• HNSCC: criteria were revised to add “non-nasopharyngeal”, and added that dose is in adults and for Opdivo used as a single agent.</li> <li>• Hepatocellular carcinoma: new indication added.</li> <li>• Melanoma criteria were revised to add that advanced includes Stage III or IV disease because guidelines recommend Opdivo use as adjuvant therapy. Dosing was revised to add 3 mg/kg every 2 weeks as a single agent.</li> <li>• MSI-H or dMMR metastatic CRC: New indication added.</li> <li>• NSCLC: criteria were revised to add that Opdivo is used as a single agent. Criteria were divided into non-squamous cell and squamous cell histologies. For non-squamous cell histologies, the list of targeted therapies used for each aberration was removed; testing for both EGFR <u>and</u> ALK is required; testing for ROS1 was removed; EGFR and ALK are negative was added as an option after testing; and criteria were added for testing for PD-L1 expression for Keytruda. For squamous cell carcinoma, criteria were added for testing for PD-L1 expression for Keytruda. See policy for details. Dosing is for single agent Opdivo. In Labs/Diagnostics, testing for PD-L1 expression for Keytruda was added. Testing for ROS1 rearrangements was removed.</li> <li>• RCC: criteria were revised to add that Opdivo will be used as a single agent and in patients with clear-cell histology Cabometyx was added to the list of options tried and Nexavar was removed from the list. The dose is in adults and for single-agent Opdivo.</li> <li>• Urothelial Carcinoma: criteria were revised to add that Opdivo is single-agent therapy, and the dose is for single agent Opdivo.</li> <li>• SCLC: added that the first option is for single-agent Opdivo.</li> <li>• Other Uses with Supportive Evidence: New indications were added for Brain Metastases Due to Melanoma, Malignant Pleural Mesothelioma, and Merkel Cell Carcinoma.</li> </ul>	11/15/2017
Update	<ul style="list-style-type: none"> <li>• 01/17/2018</li> <li>• NSCLC: criteria for PD-L1 expression testing for Keytruda were removed. Criteria require that Opdivo be used as subsequent therapy after chemotherapy and that Keytruda and Tecentriq have not been used. In Labs/Diagnostics, testing for PD-L1 expression for Keytruda was removed.</li> </ul>	N/A
Selected Revision	<ul style="list-style-type: none"> <li>• NSCLC: criteria for PD-L1 expression testing for Keytruda were removed. Criteria require that Opdivo be used as subsequent therapy after chemotherapy and that Keytruda and Tecentriq have not been used. In Labs/Diagnostics, testing for PD-L1 expression for Keytruda was removed.</li> </ul>	01/24/2018
Early Annual Revision	<ul style="list-style-type: none"> <li>• Dosing: Throughout the FDA approved indications, the dosing regimens were revised to be 240 mg every 2 weeks or 480 mg every 4 weeks given over 30 minutes for the single-agent doses of Opdivo. The MSI-H or dMMR metastatic CRC dose is 240 mg every 2 weeks (i.e., no every 4 weeks dosing). Previously most of the doses were mg per kg and/or every 2 weeks. When Opdivo is used in combination with Yervoy, the dose of Opdivo is in mg per kg.</li> <li>• cHL: Criteria were revised to include patients <math>\geq 18</math> years of age who have one of the following: the patient has had an auto-HSCT and post-transplant Adcetris therapy, the patient has had <math>\geq 3</math> lines of systemic therapy and this includes an auto-HSCT as one line of therapy, or the patient is ineligible for transplant.</li> <li>• Melanoma: Added approval criteria for adjuvant therapy in a patient with lymph node involvement or metastatic disease who has undergone complete resection. For adjuvant therapy, approval is for up to 12 months total.</li> <li>• MSI-H or dMMR CRC: Removed criterion that CRC is MSI-H or dMMR since this is in the indication.</li> <li>• RCC: For predominant clear-cell histology, criteria were added for first-line use or subsequent therapy in combination with Yervoy. Also Nexavar was added to the list of options tried. Criteria for non-clear cell history remains the same as single-agent therapy.</li> <li>• Anal Carcinoma: New indication was added based on NCCN guidelines.</li> <li>• Brain Metastases Due to Melanoma: Criteria were revised to add patients newly diagnosed with asymptomatic metastases.</li> <li>• Melanoma, Uveal: New indication was added based on NCCN guidelines.</li> <li>• Merkel Cell Carcinoma: The 240 mg every 2 weeks dosage was removed. Reference (abstract) removed.</li> </ul>	06/13/2018
Early Annual Revision	<p><b>All Indications</b></p> <ul style="list-style-type: none"> <li>• Changed approval duration to 1 year (previously was 6 months).</li> </ul>	01/30/2019

	<ul style="list-style-type: none"> <li>• Removed response criteria for continuation of therapy (now must meet PA criteria for reauthorization).</li> <li>• Removed requirement in dosing section that Opdivo is infused over 30 minutes.</li> </ul> <p><b>Brain Metastases Due to Melanoma, Uveal Melanoma, Patient has been Started on Opdivo</b></p> <ul style="list-style-type: none"> <li>• Conditions were deleted and are now generally included under melanoma. For patients already started on Opdivo, patients must meet criteria and dosing for continuation of therapy.</li> </ul> <p><b>Classic Hodgkin Lymphoma</b></p> <ul style="list-style-type: none"> <li>• Since multiple therapies or stem cell transplant is required, delete requirement that the patient has relapsed or progressive disease (presumed to be relapsed or recurrent if multiple therapies has been tried).</li> <li>• Remove criterion that requires Opdivo be administered as a single agent (not needed).</li> <li>• To align with Keytruda policy, remove criterion that limits use of Opdivo to adults.</li> <li>• For an exception to the requirement that the patient is required to have tried 3 previous lines of therapy, remove requirement that patients undergoing stem cell transplantation must undergo an autologous procedure (allogeneic procedures also mentioned in guidelines). To align with guidelines, remove requirement that the patient received post-transplant therapy with Adcetris.</li> </ul> <p><b>Head and Neck Squamous Cell Carcinoma (HNSCC)</b></p> <ul style="list-style-type: none"> <li>• Since chemotherapy is required unless contraindicated, delete requirement that the patient has recurrent or metastatic disease (presumed to be recurrent or metastatic if chemotherapy has been tried).</li> <li>• Remove criterion that required the patient has disease progression on or after trying platinum-containing chemotherapy. For the criterion that requires a previous trial of chemotherapy, add cisplatin and carboplatin to the list of examples.</li> </ul> <p><b>Hepatocellular Carcinoma, Including Hepatobiliary Cancers</b></p> <ul style="list-style-type: none"> <li>• Clarify that this condition includes hepatobiliary cancers.</li> <li>• Remove criterion that requires Opdivo be administered as a single agent (not needed).</li> <li>• Reword criteria to approve if the patient has tried at least one tyrosine kinase inhibitor with Nexavar and Lenvima listed as examples (previously specifically required a trial of Nexavar).</li> </ul> <p><b>Melanoma</b></p> <ul style="list-style-type: none"> <li>• Add a note to clarify that the criteria apply to cutaneous melanoma, brain metastasis due to melanoma, and uveal melanoma.</li> <li>• Clarify that patients without evidence of disease following resection of node-positive disease, locoregional recurrence, or in transit recurrence are examples of patients who may receive adjuvant therapy.</li> <li>• For weight-based dosing, adjust approval to allow for approval of up to 1 mg/kg dose (previously required dose to be 1 mg/kg).</li> </ul> <p><b>Colon or Rectal Cancer, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors</b></p> <ul style="list-style-type: none"> <li>• When chemotherapy is required, delete requirement that the patient has unresectable or metastatic disease (presumed to be unresectable or metastatic if chemotherapy has been tried).</li> <li>• Remove criterion that requires Opdivo be administered as a single agent (not needed).</li> <li>• Simplify criteria to require a previous trial of chemotherapy (previously required progression while on a fluoropyrimidine or adjuvant therapy with FOLFOX). Remove requirement that patients who progressed after treatment with a fluoropyrimidine have not previously been treated with Keytruda or Opdivo.</li> <li>• Add weight-based dosing to approve up to 3 mg/kg every 2 or 3 weeks.</li> </ul> <p><b>Non-Small Cell Lung Cancer</b></p> <ul style="list-style-type: none"> <li>• When chemotherapy is required, delete requirement that the patient has metastatic disease (presumed to be metastatic if chemotherapy has been tried).</li> <li>• Remove criterion that requires Opdivo be administered as a single agent (not needed).</li> <li>• Remove requirement that the patient has not previously been treated with Tecentriq, Keytruda, or Opdivo.</li> <li>• For non-squamous cell carcinoma, change criteria so that patients with unknown status for targetable mutations are not required to undergo testing (aligns with guidelines).</li> </ul> <p><b>Urothelial Carcinoma</b></p> <ul style="list-style-type: none"> <li>• Delete requirement that the patient has recurrent, locally advanced, or metastatic disease (presumed to be unresectable or metastatic if systemic therapies such as chemotherapy have been tried).</li> </ul>	
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	<ul style="list-style-type: none"> <li>Remove criterion that requires Opdivo be administered as a single agent (not needed).</li> <li>Reword criteria to require a previous trial of at least one systemic agent such as cisplatin, carboplatin, gemcitabine, or another PD-1 blocker. Criteria previously required disease progression during or after trying one of these therapies.</li> </ul> <p><b>Renal Cell Carcinoma</b></p> <ul style="list-style-type: none"> <li>Update examples of advanced disease to include metastatic disease as noted in the guidelines (previously required to be one of the listed examples).</li> <li>Remove criterion that manages use of Opdivo in combination with Yervoy (note: new Yervoy CC policy will manage Yervoy utilization in RCC).</li> <li>For weight-based dosing, adjust approval to allow for approval of up to 3 mg/kg dose (previously required dose to be 3 mg/kg).</li> </ul> <p><b>Small Cell Lung Cancer</b></p> <ul style="list-style-type: none"> <li>Move from off-label to FDA-approved indications.</li> <li>Criteria changed to require at least one systemic chemotherapy within the past 6 months, with cisplatin, carboplatin, and etoposide listed as examples (previously disease was required to have relapsed or progressed while on a platinum-containing chemotherapy).</li> <li>In dosing, add 240 mg Q2W as an approvable dose (FDA-approved dose). For weight-based dosing, adjust approval to allow for approval of up to 3 mg/kg dose (previously required dose to be 3 mg/kg). Remove requirement that Yervoy be administered in combination with Opdivo when given as weight-based dosing.</li> </ul> <p><b>Anal Carcinoma</b></p> <ul style="list-style-type: none"> <li>Since chemotherapy is required, delete requirement that the patient has metastatic disease (presumed to be metastatic if chemotherapy has been tried).</li> <li>Remove criterion that requires Opdivo be administered as a single agent (not needed).</li> </ul> <p><b>Malignant Pleural Mesothelioma</b></p> <ul style="list-style-type: none"> <li>Since chemotherapy is required, delete requirement that the patient has unresectable disease (presumed to be a form of advanced disease if chemotherapy has been tried).</li> <li>Adjust approval to allow for authorization of up to 3 mg/kg dose (previously required dose to be 3 mg/kg).</li> </ul> <p><b>Other Cancer-Related Indications</b> Add T-cell lymphoproliferative disorders, extranodal NK/T-cell lymphoma, nasal type, chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), and gestational trophoblastic neoplasia to the list of oncology indications that are reviewed on a case-by-case basis by the Medical Director.</p>	
Annual revision	<p><b>All Indications:</b> For Dosing, added “not more frequently than” with regards to frequency. Instead of “Opdivo is prescribed by...” changed to “The medication is prescribed by..” Where applicable, prescribing physician was changed to prescriber.</p> <p><b>Non-Small Cell Lung Cancer:</b> Added criteria “The patient has not progressed on prior therapy with a PD-1/PD-L1 inhibitor.”</p> <p><b>Small Cell Lung Cancer:</b> Deleted criteria requiring chemotherapy to be tried “within the past 6 months.”</p> <p><b>Gestational Trophoblastic Neoplasia:</b> Added new approval condition and criteria.</p> <p><b>Small Bowel Adenocarcinoma:</b> Added new approval condition and criteria.</p> <p><b>Other Cancer-Related Indications:</b> Deleted condition to be in-line with other policies.</p>	12/18/2019
Selected Revisions	<p><b>Non-Small Cell Lung Cancer:</b> Added criteria for use of Opdivo as first-line therapy. Added additional dosing regimens to dosing criteria.</p> <p><b>Hepatocellular Carcinoma:</b> Added additional dosing regimen to Dosing criteria.</p> <p><b>Colon or Rectal Cancer:</b> Added additional dosing regimen to Dosing criteria.</p> <p><b>Esophageal Squamous Cell Carcinoma:</b> Added new approval condition and criteria.</p> <p><b>Extranodal NK/T-Cell Lymphoma, Nasal Type:</b> Added new approval condition and criteria.</p>	06/24/2020

NSCLC – Non-small cell lung cancer; cHL – Classic Hodgkin lymphoma; RCC – Renal cell carcinoma; HNSCC – Head and neck squamous cell carcinoma; SCLC – Small cell lung cancer; MSI-H – Microsatellite instability-high; dMMR – Mismatch repair deficient; CRC – Colorectal cancer; EGFR – Epidermal growth factor receptor; ALK – Anaplastic lymphoma kinase; PD-L1 – Programmed death-ligand 1; auto-HSCT – Autologous-hematopoietic stem cell transplantation; NCCN – National Comprehensive Cancer Network.