JOHNS HOPKINS MEDICINE / JOHNS HOPKINS HEALTHCARE	Johns Hopkins HealthCare LLC **Pharmacy Public** **Medical Management Drug Policies**	*Policy Number*	MMDP053
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	Subject **Opdivo**	*Revision Date*	04/20/2022
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This document applies to the following Participating Organizations:

US Family Health Plan

Keywords: Opdivo

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I. POLICY

A. Opdivo (nivolumab) will require prior authorization for medical benefit coverage to ensure appropriate use. The process for initiating a prior authorization request can be found in policy PHARM 20.

II. POLICY CRITERIA

A. Opdivo may be approved for patients who meet the following:
   1. Cutaneous Melanoma
      a. Documentation has been submitted showing that Opdivo will be used in one of the following clinical situations:
         I. Monotherapy or in combination with ipilimumab for 4 doses followed by monotherapy for unresectable or metastatic disease
         II. Monotherapy as adjuvant treatment of stage III or IV disease following complete resection or no evidence of disease
   2. Non-Small Cell Lung Cancer (NSCLC)
      a. Documentation has been submitted showing the following
         I. Patient has a diagnosis of recurrent, advanced or metastatic NSCLC
         II. Opdvio will be used in one of the following clinical situations:
            - Combination with ipilimumab in a patient that does not have EGFR exon 19 deletions or L858R mutations or ALK rearrangements, as evidenced by laboratory testing (unless testing is infeasible due to insufficient tissue
            - Monotherapy for subsequent therapy
   3. Renal Cell Carcinoma
      a. Documentation has been submitted showing the following:
         I. Patient has a diagnosis of relapsed, advanced, or stage IV renal cell carcinoma
         II. Opdivo will be used in one of the following clinical situations:
            - Monotherapy for non-clear cell histology
            - Monotherapy for clear cell histology as subsequent therapy
            - Combination with ipilimumab for 4 doses followed by monotherapy for any of the following:
               - First-line therapy for poor or intermediate risk

- First-line therapy for clear cell histology and favorable risk
- Subsequent therapy for clear cell histology

- combination with cabozantinib for either of the following
  - First-line treatment.
  - Subsequent therapy for clear cell histology.

4. Classical Hodgkin Lymphoma (cHL)
   a. Documentation has been submitted showing Opdivo will be used in one of the following clinical situations:
      I. Combination with brentuximab vedotin for relapsed or refractory disease
      II. Monotherapy for patients meeting one of the following:
         - Patient has relapsed or progressed disease after 2 or more prior lines of therapy, or following hematopoietic stem cell transplant.
         - Patient has relapsed or refractory disease and is transplant-ineligible
         - Patient has relapsed or refractory disease and was heavily pretreated or experienced a decrease in cardiac function
5. Squamous Cell Carcinoma of the Head and Neck (SCCHN)
   a. Documentation has been submitted showing the following:
      I. Patient has been diagnosed with very advanced SCCHN with disease progression while on, or after platinum-containing chemotherapy
      II. Opdivo will be used as monotherapy for subsequent treatment
6. Nasopharyngeal Carcinoma (NPC)
   a. Documentation has been submitted showing the following:
      I. Patient has been diagnosed with unresectable, recurrent or metastatic NPC
      II. Opdivo will be used in combination with cisplatin and gemcitabine.
7. Urothelial Carcinoma – Bladder Cancer
   a. Documentation has been submitted showing that the Opdivo will be used as monotherapy in one of the following clinical situations:
      I. Subsequent therapy for locally advanced or metastatic disease
      II. Subsequent therapy for metastatic disease or local recurrence post-cystectomy
      III. Subsequent therapy for muscle invasive local recurrence or persistent disease in a preserved bladder
      IV. Subsequent therapy for stage II or IIIA disease and tumor is present following primary bladder preserving chemoradiation.
      V. Adjuvant therapy in members who are at high risk of recurrence after undergoing radical resection.
8. Urothelial Carcinoma – Primary Carcinoma of the Urethra
   a. Documentation has been submitted showing that the Opdivo will be used as monotherapy in either of the following clinical situations:
      I. Subsequent therapy for recurrent, locally advanced, or metastatic disease
      II. Adjuvant therapy in members who are at high risk of recurrence after undergoing radical resection
9. Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate
   a. Documentation has been submitted showing that the Opdivo will be used as monotherapy in either of the following clinical situations:
      I. Subsequent therapy for locally advanced or metastatic disease
      II. Adjuvant therapy in members who are at high risk of recurrence after undergoing radical resection
10. Colorectal Cancer
    a. Documentation has been submitted showing the following:

I. Patient has been diagnosed with advanced, metastatic, unresectable, or inoperable colorectal cancer, including appendiceal carcinoma, anal adenocarcinoma, and microsatellite-instability high or mismatch repair deficient tumors
II. Opdivo will be used as monotherapy or in combination with ipilimumab for 4 doses followed by monotherapy

11. Small Bowel Adenocarcinoma
    a. Documentation has been submitted showing the following:
        I. Patient has been diagnosed with advanced or metastatic small bowel adenocarcinoma, including advanced ampullary cancer, and microsatellite-instability high or mismatch repair deficient tumors
        II. Opdivo will be used as monotherapy or in combination with ipilimumab
12. Hepatocellular Carcinoma
    a. Documentation has been submitted showing that Opdivo will be used in combination with ipilimumab for 4 doses followed by monotherapy for subsequent treatment of hepatocellular carcinoma.
13. Uveal Melanoma
    a. Documentation has been submitted showing:
        I. Patient has been diagnosed with distant metastatic uveal melanoma
        II. Opdivo will be used as monotherapy or in combination with ipilimumab
14. Anal Carcinoma
    a. Documentation has been submitted showing Opdivo will be used as monotherapy for second-line or subsequent treatment of metastatic anal carcinoma.
15. Merkel Cell Carcinoma
    a. Documentation has been submitted showing that Opdvio will be used for one of the following:
        I. Treatment of recurrent disseminated or metastatic disease
        II. Neoadjuvant treatment
16. CNS Brain Metastases
    a. Documentation has been submitted showing Opdivo will be used in one of the following clinical situations:
        I. Monotherapy or in combination with ipilimumab in patients with melanoma
        II. Monontherapy in patients with PD-L1 positive non-small cell lung cancer
17. Gestational Trophoblastic Neoplasia
    a. Documentation has been submitted showing the following:
        I. Patient has multi-agent chemotherapy-resistant disease as well one of the following:
            • Patient has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum/etoposide-containing regimen
            • Patient has high-risk disease
        II. Opdivo will be used as monotherapy
18. Malignant Pleural Mesothelioma
    a. Documentation has been submitted showing one of the following:
        I. Opdivo will be used as first line therapy in combination with ipilimumab
        II. Opdivo will be used as subsequent therapy as a single agent or in combination with ipilimumab
19. Esophageal and Esophagogastric Junction Carcinoma
    a. Documentation has been submitted showing that Opdivo will be used in one of the following clinical situations:
        I. Monotherapy as subsequent treatment for unresectable locally advanced, recurrent or metastatic squamous cell carcinoma.

II. Postoperative therapy for residual pathologic disease after preoperative chemoradiation and complete tumor resection
III. Combination with chemotherapy as treatment for adenocarcinoma in patients that are not surgical candidate, or have unresectable locally advanced, recurrent, or metastatic disease

20. Extranodal NK/T-Cell Lymphoma, Nasal Type
    a. Documentation has been submitted showing the patient has a diagnosis of relapsed or refractory extranodal NK/T-cell lymphoma, nasal type.
21. Endometrial Carcinoma
    a. Documentation has been submitted showing:
        I. Patient has been diagnosed with recurrent, metastatic, or high risk mismatch repair deficient (dMMR) endometrial carcinoma, supported with laboratory testing
        II. Opdivo will be used as subsequent monotherapy
22. Vulvar Squamous Cell Carcinoma
    a. Documentation has been submitted showing:
        I. Patient has been diagnosed with HPV-related advanced, recurrent, or metastatic vulvar squamous cell carcinoma
        II. Opdivo will be used as subsequent monotherapy
23. Gastric Cancer
    a. Documentation has been submitted showing:
        I. Patient has been diagnosed with unresectable locally advanced, recurrent, or metastatic disease, or is not an surgical candidate
        II. Opdivo will be used in combination with chemotherapy
24. Small Cell Lung Cancer
    a. Documentation has been submitted showing Opdivo will be used as monotherapy for subsequent treatment of relapsed or progressive small cell lung cancer
25. Cervical Cancer
    a. Documentation has been submitted showing the following:
        I. Patient has PD-L1 positive (combined positive score [CPS] ≥ 1) recurrent or metastatic cervical cancer, confirmed with laboratory testing
        II. Opdivo will be used as monotherapy for second-line or subsequent treatment

III. AUTHORIZATION PERIOD/LIMITATIONS

A. Initial approval will be limited to 6 months of therapy
B. Continuation of therapy may be approved in 6-month intervals with documentation showing the patient is continuing to tolerate the regimen and there has not been disease progression while on treatment
    1. Indication-specific Limitations:
        a. Adjuvant treatment of melanoma or urothelial carcinoma: Opdivo may be approved in 6-month intervals up to a total of 12 months of therapy.
        b. Non-small cell lung cancer or malignant pleural mesothelioma: Opdivo may be approved in 6-month intervals up to a total of 24-months of therapy when used in combination with ipilimumab.

c. Renal Cell Carcinoma: Opdivo may be approved in 6-month intervals up to a total of 24-months of therapy when used in combination with cabozantinib

d. Gastric Cancer, Esophageal Cancer, and Esophagogastric Junction Carcinoma: Opdivo may be approved in 6-month intervals up to a total of 24-months of therapy when used in combination with chemotherapy

I. If used as postoperative therapy for completely resected esophageal cancer or esophagogastric junction carcinoma: Opdivo would be limited to a total of 12-months of therapy

IV. EXCLUSIONS

A. Opdivo will not be covered for the following:

1. Patients that have experienced disease progression while on programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor therapy (other than when used as second-line or subsequent therapy for metastatic or unresectable melanoma in combination with ipilimumab following progression on single agent anti-PD-1 immunotherapy)
2. Any indications or uses that are not FDA-approved, or guideline-supported

V. RECOMMENDED DOSAGE

Please refer to the FDA-approved prescribing information, or clinical guidelines, for indication-specific dosing details.

VI. CODES

Note: The following CPT/HCPCS codes are included below for informational purposes. Inclusion or exclusion of a CPT/HCPCS code(s) below does not signify or imply member coverage or provider reimbursement. The member's specific benefit plan determines coverage.

Medication	HCPCS/CPT Code
Injection, nivolumab, 1 mg	J9299

VII. REFERENCES

1. Opdivo [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 9, 2022.

VIII. APPROVALS

Signature on file at JHHC

DATE OF REVISION	SUMMARY OF CHANGE
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