Market Applicability														
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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Opdivo (nivolumab)

DRUG.00075

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Opdivo (nivolumab)

APPROVAL CRITERIA

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with colorectal cancer when the following criteria are met:

I. Individual meets **one** of the following criteria:
   A. Primary treatment as a single agent for unresectable metachronous metastases (defective mismatch repair/high microsatellite instability [dMMR/MSIH] only) and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months; **OR**
   B. Subsequent therapy as a single agent (if nivolumab or pembrolizumab not previously given) for unresectable advanced or metastatic disease (defective mismatch repair/high microsatellite instability [dMMR/MSIH] only) following previous treatment with oxaliplatin-irinotecan; **OR**
   C. Opdivo is being used in combination with ipilimumab as subsequent therapy for metastatic colorectal cancer with dMMR or MSIH mutations that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan;

AND

II. Individual has not received another PD-1 agent (for example, pembrolizumab); **AND**

III. Individual has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0-2; **AND**

IV. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with advanced hepatocellular carcinoma when the following criteria are met:

I. Opdivo is being used as a single agent; **AND**

Market Applicability														
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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II. Individual has demonstrated disease progression on or had intolerance to sorafenib; **AND**
III. Individual has a current ECOG performance status of 0-2; **AND**
IV. Individual has not received treatment with another PD-1 agent (for example, pembrolizumab); **AND**
V. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with relapsed or refractory Hodgkin lymphoma, except for those with lymphocyte-predominant Hodgkin lymphoma.

Requests for Opdivo (nivolumab) as a single agent may be approved for the treatment if individuals with malignant pleural mesothelioma when the following criteria are met:

I. Opdivo is being used as subsequent therapy; **OR**
II. Individual is ineligible for platinum-based chemotherapy, defined as having one or more of the following risk factors for platinum-based toxicity:
    A. ECOG performance status equal to 2;
    B. Glomerular filtration rate less than 60 mL/min;
    C. Hearing loss (measured at audiometry) of 25 dB at two contiguous frequencies;
    D. Grade 2 or greater peripheral neuropathy; **AND**
III. Individual has a current ECOG performance status of 0-2; **AND**
IV. Individual has not received treatment with another PD-1 agent (for example, pembrolizumab); **AND**
V. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with unresectable or metastatic melanoma (cutaneous and uveal) when the following criteria are met:

I. Opdivo is used as a single agent, or in combination with ipilimumab as first-line therapy for untreated melanoma; **OR**
II. Opdivo is used as a single agent, or in combination with ipilimumab as second-line or subsequent therapy for documented disease progression while receiving or since completing most recent therapy, if PD-1 agent not previously used; **AND**
III. Individual has a current ECOG performance status of 0-2; **AND**
IV. Individual has not received treatment with another PD-1 agent [for example, pembrolizumab]; **AND**

Market Applicability														
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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V. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) as a single agent may be approved for up to 12 months of adjuvant therapy for the treatment of individuals with resected advanced melanoma (cutaneous and uveal) when the following criteria are met:

I. The individual has resected stage IIIB, IIIC or stage IV disease; **AND**
II. Individual has a current ECOG performance status of 0-2; **AND**
III. Individual has not received treatment with another PD-1 agent (for example, pembrolizumab); **AND**
IV. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with Merkel Cell Carcinoma (MCC) when all of the following criteria are met:

I. Opdivo is being used as a single agent; **AND**
II. Presence of metastatic or recurrent locoregional MCC determined to be not amenable to definitive surgery or radiation therapy; **AND**
III. Individual has a current ECOG performance status of 0-2; **AND**
IV. Individual has not received treatment with another PD-1 agent (for example, pembrolizumab); **AND**
V. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with metastatic Non-Small Cell Lung Cancer (NSCLC) when all of the following criteria are met:

I. Opdivo is being used as a single agent; **AND**
II. Individual has demonstrated disease progression on or after platinum-containing chemotherapy; **AND**
III. Individual has not received treatment with another PD-1 agent [for example, pembrolizumab]; **AND**
IV. Individual has a current ECOG performance status of 0-2; **AND**
V. Individual is not receiving therapy for an autoimmune disease, chronic condition or interstitial lung disease with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the *first-line* treatment of individuals with stage IV or recurrent NSCLC when all of the following criteria are met:

Market Applicability														
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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I. Opdivo is being used in combination with ipilimumab; **AND**
II. Cytologically confirmed stage IV or recurrent NSCLC; **AND**
III. High tumor mutation burden (greater than or equal to 10 mutations per megabase); **AND**
IV. No sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) translations in nonsquamous carcinoma; **AND**
V. Individual has not received prior systemic therapy as primary therapy for advanced or metastatic NSCLC; prior adjuvant or neoadjuvant chemotherapy is permitted as long as the last administration of the prior regimen occurred at least 6 months prior; **AND**
VI. Individual has not received treatment with another PD-1 agent (for example, pembrolizumab); **AND**
VII. Current ECOG performance status of 0-2; **AND**
VIII. Individual is not receiving therapy for an autoimmune disease, chronic condition or interstitial lung disease with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with advanced or metastatic Renal Cell Carcinoma (RCC) when all of the following criteria are met:

I. Opdivo being used as a single agent; **AND**
II. Histologic confirmation of RCC with clear-cell component; **AND**
III. Individual has demonstrated progression after one or two prior anti-angiogenic regimens (for example, axitinib, bevacizumab, pazopanib, sorafenib, sunitinib, etc.) for treatment of advanced or metastatic disease; **AND**
IV. Individual has not received treatment with another PD-1 agent (for example, pembrolizumab); **AND**
V. Individual has a current ECOG performance status 0-2; **AND**
VI. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with an immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with intermediate or poor-risk, advanced Renal Cell Carcinoma (RCC) when all of the following criteria are met:

I. Opdivo is used in combination with ipilimumab, as first-line therapy for previously untreated RCC;
OR
II. Opdivo is used in combination with ipilimumab if no checkpoint blockade (PD-1, PD-L1, or CTLA-4) antibody treatment has been previously administered;

Market Applicability														
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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AND

III. Histologic confirmation of RCC with clear-cell component; **AND**
IV. Current ECOG performance status 0-2; **AND**
V. Not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with recurrent, unresectable or metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN) when all of the following criteria are met:

I. Opdivo is being used as a single agent; **AND**
II. Individual has demonstrated disease progression on or after platinum-containing chemotherapy; **AND**
III. Individual has not received treatment with another PD-1 agent (for example, pembrolizumab); **AND**
IV. Individual has a current ECOG performance status of 0-2; **AND**
V. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with small cell lung cancer when all the following criteria are met:

I. Opdivo is being used as a single agent, or in combination with ipilimumab, as subsequent therapy and individual meets one of the following:
   A. Demonstrated disease relapse within 6 months following complete or partial response or stable disease with initial treatment; **OR**
   B. No response with initial treatment; **OR**
   C. Primary progressive disease;

AND

II. Individual has not received treatment with another PD-1 agent (for example, pembrolizumab); **AND**
III. Individual has a current ECOG performance status of 0-2; **AND**
IV. Individual is not receiving therapy for an autoimmune disease, chronic condition or interstitial lung disease with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may be approved for the treatment of individuals with locally advanced or metastatic urothelial carcinoma when all the following criteria are met:

Market Applicability														
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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I. Opdivo is being used as a single agent; **AND**
II. Individual meets the following criteria:
   A. Has demonstrated disease progression on or after platinum-containing chemotherapy; **OR**
   B. Has demonstrated disease progression within 12 months of receiving neoadjuvant or adjuvant treatment with platinum-containing chemotherapy;

AND

III. Individual has not received treatment with another PD-1 agent (for example, pembrolizumab); **AND**
IV. Individual has a current ECOG performance status of 0-2; **AND**
V. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Opdivo (nivolumab) may **not** be approved when the above criteria are not met, including but not limited to **any** of the following:

I. Treatment used as first line therapy, except as described above; **OR**
II. Presence of human immunodeficiency virus (HIV) infection, hepatitis B virus infection, or hepatitis C virus infection; **OR**
III. The reason for treatment is other than for a diagnosis with accompanied criteria noted above.

State Specific Mandates		
State name	Date effective	Mandate details (including specific bill if applicable)
N/A	N/A	N/A

Key References:

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2. Bristol-Myers Squibb. A study to compare BMS-936558 to the physician's choice of either dacarbazine or carboplatin and paclitaxel in advanced melanoma patients that have progressed following anti-CTLA-4 therapy (CheckMate-037).

Market Applicability														
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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4. Bristol-Myers Squibb. An immune-therapy study to evaluate the effectiveness, safety and tolerability of nivolumab or nivolumab in combination with other agents in patients with advanced liver cancer. (CheckMate-040). NLM Identifier: NLM Identifier: NCT01658878. Last updated June 1, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT01658878. Accessed on June 16, 2018.
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7. Bristol-Myers Squibb. Phase 3 study of nivolumab or nivolumab plus ipilimumab versus ipilimumab alone in previously untreated advanced melanoma (CheckMate-067). NLM Identifier: NCT01844505. Last updated March 16, 2018. Available at: https://www.clinicaltrials.gov/ct2/show/NCT01844505. Accessed on June 16, 2018.
8. Bristol-Myers Squibb. An investigational immune-therapy trial of nivolumab, or nivolumab plus ipilimumab or nivolumab plus platinum-doublet chemotherapy, compared to platinum doublet chemotherapy in patients with stage IV non-small cell lung cancer (NSCLC) (CheckMate 227). NLM Identifier: NCT 02477826. Last updated February 13, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT02477826. Accessed on June 19, 2018.
9. Bristol-Myers Squibb. An investigational immune-therapy to determine the safety and effectiveness of nivolumab and daratumumab, with or without pomalidomide and dexamethasone, in patients with multiple myeloma. NLM Identifier: NCT01592370. Last updated June 5, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT01592370. Accessed on June 16, 2018.
10. Bristol-Myers Squibb. Study of BMS-936558 (nivolumab) compared to docetaxel in previously treated advanced or metastatic squamous cell non-small cell lung cancer (NSCLC) (CheckMate-017). NLM Identifier: NCT01642004. Last updated April 10, 2018. Available at: https://www.clinicaltrials.gov/ct2/show/NCT01642004?term=CheckMate-017&rank=1. Accessed on June 16, 2018.
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14. National Comprehensive Cancer Network®. NCCN Drugs & Biologic Compendium™ (electronic version). For additional information visit the NCCN website: http://www.nccn.org. Accessed on June 14, 2018.
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    - Anal Carcinoma (V.2.2018). Revised June 8, 2018.
    - Bladder Cancer (V.4.2018). Revised May 22, 2018.
    - Central Nervous System Cancers. (V.1.2018). Revised March 20, 2018.

Market Applicability														
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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- Colon Cancer (V.2.2018). Revised March 14, 2018.
- Kidney Cancer (V.4.2018). Revised April 23, 2018.
- Head and Neck Cancers (V.2.2018). Revised February 15, 2018.
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- Hodgkin lymphoma (V.3.2018). Revised April 16, 2018.
- Malignant Pleural Mesothelioma (V.2.2018). Revised February 26, 2018.
- Melanoma (cutaneous) (V.2.2018). Revised January 19, 2018.
- Merkel Cell Carcinoma (V.1.2018). Revised September 18, 2017.
- Non-Small Cell Lung Cancer (V.5.2018) Revised June 27, 2018.
- Rectal Cancer (V.1.2018). Revised March 14, 2018.
- Small Cell Lung Cancer (V.2.2018). Revised January 17, 2018.
- Uveal Melanoma. (V.1.2018. Revised March 15, 2018.

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