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

*FHK- Florida Healthy Kids

Keytruda (pembrolizumab)

DRUG.00071

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Keytruda (pembrolizumab)

APPROVAL CRITERIA

Cervical Cancer:

Requests of Keytruda (pembrolizumab) may be approved for the treatment of individuals with recurrent or metastatic cervical cancer when the following criteria are met:

I. Keytruda is being used as a single agent; **AND**
II. Tumor with PD-L1 gene expression with Combined Positive Score (CPS) of greater than or equal to 1; **AND**
III. Individual has not received another PD-1 agent (for example, nivolumab); and
IV. Current Eastern Cooperative Oncology Group (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.

Colorectal Cancer:

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

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

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

*FHK- Florida Healthy Kids

B. Subsequent therapy as a single agent (if nivolumab or pembrolizumab not previously given) for unresectable advanced or metastatic disease (dMMR/MSIH only) following previous treatment with one of the following:
    1. Oxaliplatin-irinotecan and fluoropyrimidine-based therapy; **OR**
    2. Oxaliplatin-irinotecan; **AND**

III. Individual has not received another PD-1 agent (for example, nivolumab); **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.

Gastric or Gastroesophageal Junction Adenocarcinoma:

Requests for Keytruda (pembrolizumab) may be approved for the treatment of individuals with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma when the following criteria are met:

I. Keytruda is being used as a single agent; **AND**
II. Tumor with PD-L1 gene expression with (CPS) of greater than or equal to 1; **AND**
III. Individual has demonstrated disease progression on or after two or more prior lines of therapy including fluoropyrimidine and platinum-containing chemotherapy, if appropriate HER2/neu-targeted therapy; **AND**
IV. Individual has not received treatment with another PD-1 agent (for example, nivolumab); **AND**
V. Individual has a current ECOG performance status of 0-2; **AND**
VI. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Head and Neck Squamous Cell Carcinoma (HNSCC):

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

I. Keytruda 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, nivolumab); **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.

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

*FHK- Florida Healthy Kids

Hodgkin Lymphoma:

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

Malignant Pleural Mesothelioma:

Requests for Keytruda (pembrolizumab) **as a single agent** may be approved for the treatment of individuals with malignant pleural mesothelioma when the following criteria are met:

I. Keytruda 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 chemotherapy toxicity:
    A. ECOG performance status equal to 2;
    B. Glomerular filtration rate less than 60mL/min;
    C. Hearing loss (measured at audiometry) of 25dB 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, nivolumab); **AND**
V. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Melanoma (Cutaneous and Uveal):

Requests for Keytruda (pembrolizumab) may be approved for the treatment of individuals with melanoma (cutaneous and uveal) when the following criteria are met:

I. Keytruda is being used as a single agent; **AND**
II. Presence of unresectable or metastatic melanoma; **AND**
III. Treatment meets **one** of the following criteria:
    A. Used as first-line therapy in untreated disease; **OR**
    B. Used as second-line or subsequent therapy for documented disease progression while receiving or since completed most recent therapy;

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

*FHK- Florida Healthy Kids

AND

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

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

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

Merkel Cell Carcinoma (MCC):

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

I. Keytruda 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, nivolumab); **AND**
V. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Non-Hodgkin Lymphoma, Primary Mediastinal Large B-Cell Lymphoma:

Requests for Keytruda (pembrolizumab) may be approved for the treatment of individuals with primary mediastinal large B-cell lymphoma when the following criteria are met:

I. Keytruda is being used as single agent; **AND**
II. Treatment meets one of the following:
    A. Used for refractory disease; **OR**

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

*FHK- Florida Healthy Kids

B. Used as subsequent therapy for disease relapse after receiving two or more prior lines of therapy; **AND**

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

Non-Small Cell Lung Cancer:

Requests for Keytruda (pembrolizumab) may be approved for the first-line treatment of advanced (metastatic) Non-Small Cell Lung Cancer (NSCLC) when the following criteria are met:

I. Keytruda is being used as a single agent; **AND**
II. Cytologically confirmed stage IV NSCLC; **AND**
III. Tumor expresses PD-L1 gene on at least 50% of tumor cells; **AND**
IV. No sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) translocations in nonsquamous carcinoma; **AND**
V. Individual has not received another PD-1 agent (for example, nivolumab) and has not undergone previous systemic therapy for metastatic disease; **AND**
VI. Individual has a current ECOG performance status of 0-2; **AND**
VII. Individual is not receiving therapy for an autoimmune disease, chronic condition or interstitial lung disease with a systemic immunosuppressant.

Requests for Keytruda (pembrolizumab) may be approved for the first-line treatment of advanced or metastatic nonsquamous NSCLC when the following criteria are met:

I. Keytruda is being used in combination with pemetrexed and a platinum agent; **AND**
II. Cytologically confirmed stage IIIb or IV NSCLC; **AND**
III. No sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) translocations; **AND**
IV. Individual has not received another PD-1 agent (for example, nivolumab) and has not undergone previous systemic therapy for metastatic disease; **AND**
V. Individual has a current ECOG performance status of 0-2; **AND**
VI. Individual is not receiving therapy for an autoimmune disease, chronic condition or interstitial lung disease with a systemic immunosuppressant.

Requests for Keytruda (pembrolizumab) may be approved for continuation maintenance therapy of recurrent or metastatic nonsquamous NSCLC when 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

*FHK- Florida Healthy Kids

I. Keytruda is being used in combination with pemetrexed as **continuation maintenance therapy**, if given first-line as part of pembrolizumab/pemetrexed and platinum-based regimen; **AND**
II. Individual has achieved tumor response or stable disease following initial cytotoxic therapy; **AND**
III. Individual has not received another PD-1 agent (for example, nivolumab); **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 Keytruda (pembrolizumab) may be approved for continuation maintenance therapy of recurrent or metastatic squamous cell NSCLC when **all** of the following criteria are met:

I. Keytruda is being used as a single-agent as **continuation maintenance therapy**, if given first-line as part of pembrolizumab/carboplatin/paclitaxel regimen; **AND**
II. Individual has achieved tumor response or stable disease following initial cytotoxic therapy; **AND**
III. Individual has not received another PD-1 agent (for example, nivolumab); **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 Keytruda (pembrolizumab) may be approved for the treatment of metastatic NSCLC as a second or subsequent line of therapy when the following criteria are met:

I. Keytruda is being used as a single agent; **AND**
II. Tumor with PD-L1 gene expression level greater than or equal to 1% with demonstrated disease progression on or after platinum-containing chemotherapy; **AND**
III. When anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) genomic tumor aberrations are present, must have demonstrated disease progression on U.S. Food and Drug Administration (FDA) approved therapy for the aberrations prior to receiving pembrolizumab; **AND**
IV. Individual has not received another PD-1 agent (for example, nivolumab); **AND**
V. Individual has a current ECOG performance status of 0-2; **AND**
VI. Individual is not receiving therapy for an autoimmune disease, chronic condition or interstitial lung disease with a- systemic immunosuppressant.

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

*FHK- Florida Healthy Kids

Solid Tumors:

Requests for Keytruda (pembrolizumab) may be approved for the treatment of unresectable or metastatic solid tumors (dMMR/MSIH only) when the following criteria are met:

I. Keytruda is being used as a single agent; **AND**
II. Individual has demonstrated disease progression following prior treatment with no other satisfactory alternative treatment options; **AND**
III. Individual has not received another PD-1 agent (for example, nivolumab); **AND**
IV. Individual's 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.

Urothelial Carcinoma:

Requests for Keytruda (pembrolizumab) may be approved for the treatment of locally advanced or metastatic urothelial carcinoma when the following criteria are met:

I. Keytruda is being used as a single agent; **AND**
II. Treatment meets **one** of the following criteria:
   A. Individual is not eligible for any platinum-containing chemotherapy, and if cisplatin-ineligible, tumor expresses PD-L1 with CPS of greater than or equal to 10; **OR**
   B. Individual has demonstrated disease progression on or after platinum-containing chemotherapy; **OR**
   C. Individual has demonstrated disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy;

AND

III. Individual has not received another PD-1 agent (for example, nivolumab); **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 Keytruda (pembrolizumab) may **not** be approved when the above criteria are not met, including but not limited to any of the following:

I. Presence of human immunodeficiency virus (HIV) infection, hepatitis B virus infection, or hepatitis C virus infection; **OR**
II. The reason for treatment is other than for a diagnosis with accompanied criteria noted above.

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

*FHK- Florida Healthy Kids

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

Key References:

1. American Cancer Society. Cancer facts & figures 2018. Atlanta: American Cancer Society; 2018. Available at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf. Accessed on June 8, 2018.
2. American Cancer Society. Key statistics for bladder cancer. Revised on January 5, 2017. Available at: https://www.cancer.org/cancer/bladder-cancer/about/key-statistics.html. Accessed on June 08, 2018.
3. Hanna N, Johnson D, Temin S, et al. Systemic Therapy for Stage IV Non-Small-Cell Lung Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Oncol Pract. 2017; 13(12):832-837.
4. Keytruda [Product Information]. Whitehouse Station, NJ. Merck Sharp & Dohme Corp.; June 19, 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125514s043lbl.pdf. Accessed on July 9, 2018.
5. Merck Sharp & Dohme Corp. A trial of pembrolizumab (MK-3475) in participants with blood cancers (MK-3475-013) (KEYNOTE-013). NLM Identifier: NCT01953692. Last updated December 19, 2017. Available at: https://clinicaltrials.gov/ct2/show/NCT01953692. Accessed on June 08, 2018.
6. Merck Sharp & Dohme Corp. Study of pembrolizumab (MK-3475) compared to platinum-based chemotherapies in participants with metastatic non-small cell lung cancer (MK-3475-024/KEYNOTE-024). NLM Identifier: NCT02142738. Last updated March 16, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT02142738?term=KEYNOTE-024&rank=1. Accessed on June 08, 2018.
7. Merck Sharp & Dohme Corp. Study of pembrolizumab (MK-3475) in participants with advanced solid tumors (MK-3475-012/KEYNOTE-012). NLM Identifier: NCT01848834. Last updated March 14, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT01848834. Accessed on June 08, 2018.
8. Merck Sharp & Dohme Corp. Study of pembrolizumab (MK-3475 in participants with advanced solid tumors (MK-3475-158/KEYNOTE-158). NLM Identifier: NCT02628067. Last updated June 8, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT02628067. Accessed on June 15, 2018.
9. Merck Sharp & Dohme Corp. Study of pembrolizumab (MK-3475) in participants with progressive locally advanced or metastatic carcinoma, melanoma, or non-small cell lung carcinoma (P07990/MK-3475-001/KEYNOTE-001). NLM Identifier: NCT01295827. Last updated on March 16, 2018. Available at: http://clinicaltrials.gov/ct2/show/NCT01295827?term=01295827&rank=1. Accessed on June 28, 2018.
10. National Cancer Institute. Common terminology criteria for adverse events. Version 4.03. June 2010. Available at: https://www.eortc.be/services/doc/ctc/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf. Accessed on June 09, 2018.
11. National Comprehensive Cancer Network®. NCCN Drugs & Biologic Compendium™ (electronic version). For additional information visit the NCCN website: http://www.nccn.org. Accessed on July 9, 2018.
12. National Comprehensive Cancer Network® NCCN Clinical Practice Guidelines in Oncology™. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on July 9, 2018.
    - Anal Carcinoma (V.2.2018). Revised June 8, 2018.
    - B-Cell Lymphomas (V.4.2018). Revised May 15, 2018.
    - Bladder Cancer (V.5.2018). Revised July 3, 2018.
    - Colon Cancer (V.2.2018). Revised March 14, 2018.
    - Central Nervous System Cancers. (V.1.2018) Revised March 20, 2018.
    - Head and Neck Cancer (V.2.2018) Revised February 15, 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

*FHK- Florida Healthy Kids

- 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 26, 2018.
- Ovarian Cancer (V.2.2018) Revised March 9, 2018.
- Rectal Cancer (V.1.2018). Revised March 14, 2018.
- Small Cell Lung Cancer (V.2.2018). Revised January 17, 2018.
- T-Cell Lymphomas. (V.4.2018). Revised May 14, 2018.
- Testicular Cancer (V.2.2018). Revised February 16, 2018.
- Uveal Melanoma. (V.1.2018). Revised March15. 2018.

13. Pembrolizumab Monograph. Lexicomp® Online, American Hospital Formulary Services® (AHFS®) Online, Hudson, Ohio, Lexi-Comp., Inc. Last revised August 31, 2017. Accessed on June 08, 2018.
14. Pembrolizumab (systemic). In: DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated May 21, 2018. Available at: http://www.micromedexsolutions.com. Accessed on June 08, 2018.
15. U.S. Food and Drug Administration. Keytruda (pembrolizumab) or Tecentriq (atezolizumab): FDA alerts health care professionals and investigators: FDA statement - decreased survival in some patients in clinical trials associated with monotherapy. May 18, 2018. Available at: https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm608253.htm. Accessed on July 26, 2018.