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Subject: Pembrolizumab (Keytruda®) Injection

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DESCRIPTION:

Pembrolizumab is a human monoclonal antibody that binds to the programmed death receptor (PD-1) on T-cells to block the interaction with PD-ligands, PD-L1 and PD-L2, on the tumor cell. The interaction of PD-1 with these ligands contributes to inhibition of active T-cell immune surveillance of tumors. Upregulation of PD-L1 occurs in some tumors and can further contribute to decreased immune response. Through binding of PD-1, pembrolizumab prevents inhibition of the anti-tumor immune response.

Pembrolizumab (Keytruda) was initially approved by the U.S. Food and Drug Administration (FDA) in September 2014 for the treatment of unresectable or metastatic melanoma. Pembrolizumab was granted FDA approval in October 2015 for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express programmed death ligand 1 (PD-L1) with a Tumor Proportion Score (TPS) greater than or equal to 1% and who have disease progression on or after platinum-containing chemotherapy. Additionally, the product is approved for use in patients with metastatic NSCLC epithelial growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) gene rearrangements in patients who have disease progression on FDA-approved targeted therapy prior to receiving pembrolizumab. A companion diagnostic test was approved to detect PD-L1 expression in non-small cell lung tumors. The FDA expanded the use in metastatic NSCLC for the treatment of tumors with high-PD-L1 expression (TPS greater than or equal to 50%) with no prior systemic chemotherapy and no EGFR or ALK genomic tumor aberrations. Pembrolizumab received approval for metastatic nonsquamous NSCLC as initial therapy in combination with pemetrexed and carboplatin and for metastatic squamous NSCLC as initial therapy in combination with carboplatin and either paclitaxel or nab-paclitaxel. Pembrolizumab has also been FDA-approved for patients with recurrent or metastatic squamous cell carcinoma of the

head and neck, refractory or relapsed Classical Hodgkin Lymphoma, cervical cancer, esophageal cancer, gastric cancer, hepatocellular carcinoma, Merkel cell carcinoma, primary mediastinal large B-cell lymphomas, small cell lung cancer, locally advanced or metastatic urothelial carcinoma, unresectable or metastatic microsatellite instability high (MSI-H) solid tumors or colorectal cancer, and adjuvant treatment of melanoma. These additional indications are approved under accelerated approval based on tumor response rate and durability of response; continued approval is contingent upon results in confirmatory trials.

National Comprehensive Cancer Network (NCCN) Guidelines recommend pembrolizumab for the treatment of adrenocortical carcinoma, anal cancer, bile duct cancer, bladder cancer, cervical cancer, brain metastases, bone cancer, Classical Hodgkin Lymphoma, colon and rectal cancer, endometrial carcinoma, esophageal cancer, Extranodal NK/T-cell lymphomas, gallbladder cancer, gastric cancer, Gestational Trophoblastic Neoplasia, head and neck cancer, hepatocellular cancer, kidney cancer, malignant pleural mesothelioma, melanoma, Merkel Cell carcinoma, mycosis fungoides/sezary syndrome, neuroendocrine tumors, non-small cell lung cancer, ovarian cancer, pancreatic cancer, penile cancer, primary mediastinal large B-cell lymphomas, prostate cancer, small bowel adenocarcinoma, small cell lung cancer, testicular cancer, thymic carcinomas, uveal melanoma and vulvar cancer.

POSITION STATEMENT:

I. Initiation of pembrolizumab (Keytruda) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions in Table 1 when **ALL** of the indication specific criteria are met:

Table 1

Indication	Specific Criteria
Adrenocortical carcinoma (Adrenal gland tumor)	When **ALL** of the following are met: 1. Member has unresectable or metastatic disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab is used as subsequent therapy after disease progression on initial treatment 4. Member has no alternative treatment options 5. Pembrolizumab will be used as monotherapy 6. Dose does not exceed the maximum FDA-approved dosing*
Anal cancer	When **ALL** of the following are met: 1. Member's disease is metastatic 2. Member has squamous cell carcinoma 3. Member's disease progressed on initial chemotherapy 4. Pembrolizumab will be used as a single agent 5. Dose does not exceed the maximum FDA-approved dosing*
Bladder cancer (also includes cancer of the urethra, upper genitourinary tract,	When **ALL** of the following are met: 1. Member is diagnosed with locally advanced or metastatic urothelial carcinoma 2. Member's meets **ONE** of the following: a. Disease progressed on or after platinum-based therapy (e.g., cisplatin

and prostate)	or carboplatin) b. Disease progressed within 12 months of neoadjuvant or adjuvant treatment with platinum-based therapy c. Member is not eligible for cisplatin therapy and has PD-L1 expression detected by an FDA-approved test with a combined positive score (CPS) of ≥10 d. Member is not eligible for any platinum based chemotherapy (e.g., cisplatin, carboplatin) 3. Pembrolizumab will be used as a single agent 4. Dose does not exceed 200 mg every 3 weeks
Bone Cancer (includes Ewing sarcoma, mesenchymal chondrosarcoma, osteosarcoma, dedifferentiated chondrosarcoma, high-grade undifferentiated pleomorphic sarcoma (UPS))	When **ALL** of the following are met: 1. Member has unresectable or metastatic disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab is used as subsequent therapy after disease progression on initial treatment 4. Member has no alternative treatment options 5. Pembrolizumab will be used as monotherapy 6. Dose does not exceed the maximum FDA-approved dosing*
Brain metastases from melanoma or non-small cell lung cancer	When **ALL** of the following are met: 1. Pembrolizumab is used for **ONE** of the following: a. Brain metastases from melanoma b. Brain metastases from non-small cell lung cancer and PD-L1 expression is detected by an FDA-approved test with Tumor Proportion Score (TPS) ≥1% 2. Pembrolizumab will be used as a single agent 3. Dose does not exceed 200 mg every 3 weeks
Cholangiocarcinoma (bile duct cancer)	When **ALL** of the following are met: 1. Member has unresectable or metastatic disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab will be used as monotherapy 4. Dose does not exceed the maximum FDA-approved dosing*
Classical Hodgkin Lymphoma (CHL)	When **ALL** of the following are met: 1. Member has relapsed or refractory disease 2. Pembrolizumab will be used as monotherapy 3. Dose does not exceed the maximum FDA-approved dosing*
Cervical cancer	When **ALL** of the following are met: 1. Member has recurrent or metastatic disease 2. Pembrolizumab is used as subsequent therapy after disease progression on initial treatment 3. **ONE** of the following:

	a. Member's tumor has PD-L1 expression detected by an FDA-approved test with a combined positive score (CPS) of ≥1% b. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 4. Pembrolizumab will be used as monotherapy 5. Dose does not exceed 200 mg every 3 weeks
Colon or Rectal cancer	When **ALL** of the following are met: 1. Member has metastatic or unresectable advanced disease 2. Tumor is classified as microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) 3. The member has not previously received pembrolizumab or nivolumab therapy 4. **ONE** of the following a. As subsequent therapy following disease progression with oxaliplatin-, irinotecan- or fluoropyrimidine-based therapy b. Initial therapy in members who are not candidates for more intensive therapy c. Following adjuvant FOLFOX or CapeOX if received within the previous year 5. Pembrolizumab will be used as monotherapy 6. Dose does not exceed the maximum FDA-approved dosing*
Endometrial Carcinoma	When **ALL** of the following are met: 1. Member has recurrent, metastatic, or high risk disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab is used as subsequent therapy after disease progression on initial treatment 4. Pembrolizumab will be used as monotherapy 5. Dose does not exceed the maximum FDA-approved dosing*
Esophageal cancer	When **ALL** of the following are met: 1. **ONE** of the following: a. Member has unresectable locally advanced disease b. Member has recurrent or metastatic disease c. Member is not a surgical candidate 2. **ONE** of the following: a. Pembrolizumab is used as second-line or subsequent therapy after disease progression on initial treatment and member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] b. Pembrolizumab is used as second line or greater therapy and member's tumor has PD-L1 expression detected by an FDA-approved test with a combined positive score (CPS) of ≥10% c. Pembrolizumab is used as third line or greater therapy and member's tumor has PD-L1 expression detected by an FDA-approved test with a combined positive score (CPS) of ≥1% 3. Member's ECOG performance status is 0-2 or KPS is greater than or equal to 60%

	4. Pembrolizumab will be used as monotherapy 5. Dose does not exceed 200 mg every 3 weeks
Extranodal NK/T-cell lymphomas	When **ALL** of the following are met: 1. Member has relapsed or refractory disease 2. Member has an inadequate response or contraindication to asparaginase-based therapy (e.g., pegaspargase) 3. Pembrolizumab will be used as monotherapy 4. Dose does not exceed 2 mg/kg every 3 weeks
Gallbladder cancer	When **ALL** of the following are met: 1. Member has unresectable or metastatic disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab will be used as monotherapy 4. Dose does not exceed the maximum FDA-approved dosing*
Gastric or gastroesophageal junction cancer	When **ALL** of the following are met: 1. **ONE** of the following: a. Member has unresectable locally advanced disease b. Member has recurrent or metastatic disease c. Member is not a surgical candidate 2. **ONE** of the following: a. Pembrolizumab is used as second-line or subsequent therapy after disease progression on initial treatment and member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] b. Pembrolizumab is used as third line or greater therapy and member's tumor has PD-L1 expression detected by an FDA-approved test with a combined positive score (CPS) of $\geq$1% 3. Member's ECOG performance status is 0-2 or KPS is greater than or equal to 60% 4. Pembrolizumab will be used as monotherapy 5. Dose does not exceed 200 mg every 3 weeks
Gestational Trophoblastic Neoplasia	When **ALL** of the following are met: 1. Member has recurrent or progressive disease 2. **ONE** of the following: a. Member was previously treated with a platinum/etoposide-containing regimen b. Member has methotrexate-resistant high-risk disease 3. Pembrolizumab will be used as monotherapy 4. Dose does not exceed the maximum FDA-approved dosing*
Hepatocellular cancer	When ALL of the following are met: 1. Member's disease progressed on first line systemic treatment 2. Member has Child-Pugh Class A disease 3. **ONE** of the following: a. Unresectable disease and is not a candidate for transplant

	b. Metastatic disease c. Inoperable due to performance status or comorbidities and has local disease d. Extensive tumor burden 4. Pembrolizumab will be used as monotherapy 5. Dose does not exceed 200 mg every 3 weeks
Kidney cancer	When **ALL** of the following are met: 1. Member is diagnosed with relapsed or stage IV disease with predominant clear cell histology 2. Pembrolizumab is used in combination with axitinib 3. Dose does not exceed 200 mg every 3 weeks
Malignant Pleural Mesothelioma (MPM)	When ALL of the following are met: 1. Pembrolizumab is used as subsequent therapy after disease progression with pemetrexed 2. Pembrolizumab will be used as a single agent 3. Dose does not exceed 200 mg every 3 weeks
Melanoma	When used for **ONE** of the following: 1. Treatment of unresectable or metastatic melanoma a. Member meets one of the following: i. Pembrolizumab is used as first-line therapy ii. Pembrolizumab is used as second-line or subsequent therapy for disease progression if not previously used iii. Pembrolizumab is used as reinduction therapy and **ALL** of the following: 1. Member's disease relapsed or progressed greater than 3 months after initial clinical response or stable disease with previous pembrolizumab treatment 2. Member does not have any remaining toxicity from previous pembrolizumab treatment b. Pembrolizumab will be used as monotherapy c. Dose does not exceed 200 mg every 3 weeks 2. Adjuvant treatment of melanoma a. **ONE** of the following: i. Member has Stage III disease ii. Member had complete lymph node dissection iii. Member underwent surgery for disease recurrence and has no evidence of disease following surgery iv. Member with metastatic disease who had complete resection with no evidence of disease b. Pembrolizumab will be used as a single agent c. Dose does not exceed 200 mg every 3 weeks
Merkel cell carcinoma	When **ALL** of the following are met: 1. Member's disease is classified as **ONE** of the following:

	a. Recurrent locally advanced disease b. Metastatic disease 2. Pembrolizumab will be used as monotherapy 3. Dose does not exceed the maximum FDA-approved dosing*
Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors (non-colorectal tumors)	When **ALL** of the following are met: 1. Member has unresectable or metastatic disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab is used as subsequent therapy after disease progression on initial treatment 4. Member has no alternative treatment options 5. Pembrolizumab will be used as monotherapy 6. Dose does not exceed the maximum FDA-approved dosing*
Mycosis fungoides (MF)/Sezary syndrome (SS)	When **ALL** of the following are met: 1. Member has Stage III or IV disease 2. Pembrolizumab will be used as monotherapy 3. Dose does not exceed 2 mg/kg every 3 weeks
Neuroendocrine tumors (extrapulmonary) with poorly differentiated carcinoma/large or small cell carcinoma	When **ALL** of the following are met: 1. Member has unresectable or metastatic disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab is used as subsequent therapy after disease progression on initial treatment 4. Member has no alternative treatment options 5. Pembrolizumab will be used as monotherapy 6. Dose does not exceed the maximum FDA-approved dosing*
Non-small Cell Lung Cancer (NSCLC)	When **ALL** of the following are met: 1. Member's disease is classified as ONE of the following: a. Metastatic b. Mediastinal lymph node recurrence and member has received prior radiation therapy c. Stage III disease and member is not a candidate for surgical resection or definitive chemoradiation (only when used as a single agent) 2. Member's ECOG performance status is 0-2 3. **ONE** of the following: a. Pembrolizumab is used as a single agent for **ONE** of the following: i. First line therapy if EGFR and ALK are negative or unknown and PD-L1 expression is detected by an FDA-approved test with TPS ≥ 1% ii. Subsequent therapy as a single agent if member has not previously received a checkpoint inhibitor (e.g., nivolumab, pembrolizumab, or atezolizumab) after disease progression on initial chemotherapy and PD-L1 expression is detected by an FDA-approved test with TPS ≥1%

	iii. Maintenance therapy in members who achieved tumor response or stable disease with previous pembrolizumab treatment b. Pembrolizumab is used for nonsquamous NSCLC in combination with pemetrexed and either carboplatin or cisplatin, for **ONE** of the following: i. First line therapy if EGFR and ALK are negative or unknown and PD-L1 expression is detected by an FDA-approved test with TPS ≥ 1% ii. First line therapy if EGFR, ALK, ROS1, BRAF are negative or unknown and PD-L1 TPS < 1% or unknown iii. First line or subsequent therapy if BRAF V600E mutation is positive iv. Used as subsequent therapy if not previously used for **ONE** of the following: 1. After disease progression with **ONE** of the following: a. Targeted therapy for EGFR mutation (e.g., erlotinib, afatinib, gefitinib, osimertinib, dacomitinib) b. Targeted therapy for ALK rearrangements (e.g., crizotinib, ceritinib, alectinib, brigatinib) c. Targeted therapy for ROS1 rearrangements (e.g., crizotinib, certinib) 2. PD-L1 expression detected by an FDA-approved test with TPS ≥ 1% and EGFR, ALK, and ROS1 are negative or unknown and no prior platinum-doublet chemotherapy c. Pembrolizumab is used for squamous NSCLC in combination with either carboplatin or cisplatin, and paclitaxel (or nab-paclitaxel if documented hypersensitivity to conventional paclitaxel or docetaxel) for **ONE** of the following: i. First line therapy if EGFR and ALK are negative or unknown and PD-L1 expression is detected by an FDA-approved test with TPS ≥ 1% ii. First line therapy if EGFR, ALK, ROS1, BRAF are negative or unknown and PD-L1 TPS < 1% or unknown iii. First line or subsequent therapy if BRAF V600E mutation is positive iv. Used as subsequent therapy if not previously used for **ONE** of the following: 1. After disease progression with **ONE** of the following: a. Targeted therapy for EGFR mutation (e.g., erlotinib, afatinib, gefitinib, osimertinib, dacomitinib) b. Targeted therapy for ALK rearrangements (e.g., crizotinib, ceritinib, alectinib, brigatinib) c. Targeted therapy for ROS1

	rearrangements (e.g., crizotinib, certinib) 2. PD-L1 expression detected by an FDA-approved test with TPS ≥ 1% and EGFR, ALK, and ROS1 are negative or unknown and no prior platinum-doublet chemotherapy d. Pembrolizumab is used as maintenance therapy in combination with pemetrexed in members who achieved tumor response or stable disease with previous pembrolizumab/pemetrexed with carboplatin or cisplatin 4. Dose does not exceed 200 mg every 3 weeks
Ovarian cancer (includes epithelial ovarian, fallopian tube, and primary peritoneal cancer)	When **ALL** of the following are met: 1. Member has persistent or recurrent disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab is used as subsequent therapy after disease progression on initial treatment 4. Pembrolizumab will be used as monotherapy 5. Dose does not exceed the maximum FDA-approved dosing*
Pancreatic cancer	When **ALL** of the following are met: 1. Member has locally advanced, unresectable, recurrent, or metastatic disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab is used as second-line therapy after disease progression on initial treatment 4. Member's ECOG performance status is 0-2 5. Pembrolizumab will be used as monotherapy 6. Dose does not exceed the maximum FDA-approved dosing*
Penile cancer	When **ALL** of the following are met: 1. Member has unresectable or metastatic disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. Pembrolizumab is used as subsequent therapy after disease progression on initial treatment 4. Member has no alternative treatment options 5. Pembrolizumab will be used as monotherapy 6. Dose does not exceed the maximum FDA-approved dosing*
Primary Mediastinal Large B-cell Lymphoma	When **ALL** of the following are met: 1. Member has relapsed or refractory disease 2. Pembrolizumab will be used as monotherapy 3. Dose does not exceed the maximum FDA-approved dosing*
Prostate cancer	When **ALL** of the following are met: 1. Member has metastatic castration-resistant prostate cancer 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR]

	3. Member had disease progression on initial systemic treatment 4. Member has not previously received pembrolizumab 5. Pembrolizumab will be used as monotherapy 6. Dose does not exceed the maximum FDA-approved dosing*
Squamous cell carcinoma of the Head and Neck (SCCHN)	When **ALL** of the following are met: 1. Member's disease is recurrent, unresectable or metastatic 2. **ONE** of the following: a. Member's disease progressed on or after platinum-based therapy (e.g., cisplatin or carboplatin) and pembrolizumab will be used as a single agent b. Member's tumor has PD-L1 expression detected by an FDA-approved test with a combined positive score (CPS) of ≥1% and pembrolizumab will be used as a single agent c. Pembrolizumab will be used as first-line therapy in combination with a platinum (e.g., cisplatin or carboplatin) and fluorouracil 3. Member's ECOG performance status is 0-3 4. Dose does not exceed 200 mg every 3 weeks
Small Bowel Adenocarcinoma	When **ALL** of the following are met: 1. Member has metastatic or unresectable advanced disease 2. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 3. **ONE** of the following: a. Pembrolizumab is used as subsequent therapy after disease progression on initial treatment b. Member has a contraindication to oxaliplatin c. Member has previously received oxaliplatin in the adjuvant setting 4. Pembrolizumab will be used as monotherapy 5. Dose does not exceed the maximum FDA-approved dosing*
Small Cell Lung Cancer (SCLC)	When **ALL** of the following are met: 1. **ONE** of the following: a. Member's disease relapsed within 6 months of initial chemotherapy b. Member's disease is progressive on initial chemotherapy 2. Member's ECOG performance status is 0-2 3. Pembrolizumab will be used as a single agent 4. Dose does not exceed the maximum FDA-approved dosing*
Testicular cancer	When **ALL** of the following are met: 1. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] 2. Member's disease progressed on second-line chemotherapy 3. Pembrolizumab will be used as monotherapy 4. Dose does not exceed the maximum FDA-approved dosing*
Thymic carcinoma	When **ALL** of the following are met: 1. Member's disease is locally advanced or metastatic

	2. Member's disease progressed on first line therapy 3. Pembrolizumab will be used as monotherapy 4. Dose does not exceed 200 mg every 3 weeks
Uveal melanoma	When **ALL** of the following are met: 1. Member's disease is unresectable or metastatic 2. Pembrolizumab will be used as monotherapy 3. Dose does not exceed the maximum FDA-approved dosing*
Vulvar cancer	When **ALL** of the following are met: 1. Member has advanced, recurrent or metastatic squamous cell carcinoma 2. Pembrolizumab is used as second-line or subsequent therapy after disease progression on initial treatment 3. **ONE** of the following: a. Member's tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR] b. Member's tumor has PD-L1 expression detected by an FDA-approved test with a combined positive score (CPS) of ≥1% 4. Pembrolizumab will be used as monotherapy 5. Dose does not exceed the maximum FDA-approved dosing*
Other FDA-approved or NCCN supported diagnosis (not previously listed above)	When **ALL** of the following are met: 1. **ONE** of the following is met: a. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert) b. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation 2. Dose does not exceed the maximum FDA-approved dosing*

Duration of approval: 6 months

II. Pembrolizumab (Keytruda) meets the definition of medical necessity when used for the following designated Orphan Drug indications (http://www.fda.gov/orphan/designat/list.htm) when used as a single agent and the dose does not exceed the maximum FDA-approved dosing*:

1. Follicular lymphoma

Duration of approval: 6 months

III. Continuation of pembrolizumab (Keytruda) **meets the definition of medical necessity** for the indications in Table 1 and orphan indications for members meeting the following criteria:

1. The member has been previously approved by Florida Blue or another health plan in the past 2 years, OR the member has previously met all indication-specific criteria for coverage

2. Member's disease has not progressed during treatment with pembrolizumab
3. Pembrolizumab will be used as monotherapy**
4. The dose does not exceed the following based on indication:
    a. Extranodal NK/T-cell lymphoma or Mycosis fungoides/Sezary syndrome: 2 mg/kg every 3 weeks
    b. Bladder cancer, brain metastases from melanoma or NSCLC, cervical cancer, esophageal cancer, gastric cancer, hepatocellular cancer, kidney cancer, MPM, melanoma, NSCLC, Squamous cell carcinoma of the Head and Neck, or thymic carcinomas: 200 mg every 3 weeks
    c. Adrenocortical carcinoma, anal cancer, Bone cancer, Cholangiocarcinoma, Classical Hodgkin Lymphoma, Colon or rectal cancer, endometrial cancer, gallbladder cancer, Gestational Trophoblastic Neoplasia, Merkel cell carcinoma, MSI-H/dMMR solid tumors, neuroendocrine tumors, ovarian cancer, pancreatic cancer, penile cancer, primary mediastinal large B-cell lymphoma, prostate cancer, small bowel adenocarcinoma, small cell lung cancer, testicular cancer, uveal melanoma, vulvar cancer, orphan indications and other FDA approved or NCCN supported diagnosis: does not exceed maximum FDA-approved dosing*

Duration of approval: 6 months

*__NOTE__: The maximum FDA approved dose is 200 mg every 3 weeks for adult patients and 2 mg/kg (up to 200 mg) every 3 weeks for pediatrics.

**Exception for use in combination with pemetrexed for NSCLC or in combination with axitinib for kidney cancer

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Melanoma: 200 mg IV over 30 minutes every three weeks. Continue treatment until disease progression or unacceptable toxicity occurs.
- Non-Small Cell Lung Cancer: 200 mg IV over 30 minutes every 3 weeks. Select patients for treatment based on the presence of positive PD-L1 expression. Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Small Cell Lung Cancer: 200 mg IV over 30 minutes every 3 weeks. Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Squamous cell carcinoma of the Head and Neck: 200 mg IV over 30 minutes every 3 weeks. Select patients for treatment based on the presence of positive PD-L1 expression. Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Classical Hodgkin Lymphoma: 200 mg IV over 30 minutes every 3 weeks for adult patients and 2 mg/kg IV every 3 weeks for pediatrics (up to 200 mg). Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

- Primary Mediastinal Large B-cell Lymphoma: 200 mg IV over 30 minutes every 3 weeks for adult patients and 2 mg/kg IV every 3 weeks for pediatrics (up to 200 mg). Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Urothelial carcinoma: 200 mg IV over 30 minutes every 3 weeks. Select patients for treatment based on the presence of positive PD-L1 expression. Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- MSI-H cancer: 200 mg IV over 30 minutes every 3 weeks for adult patients and 2 mg/kg IV every 3 weeks for pediatrics (up to 200 mg). Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Gastric cancer: 200 mg IV over 30 minutes every 3 weeks. Select patients for treatment based on the presence of positive PD-L1 expression. Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Esophageal cancer: 200 mg IV over 30 minutes every 3 weeks. Select patients for treatment based on the presence of positive PD-L1 expression. Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Cervical cancer: 200 mg IV over 30 minutes every 3 weeks. Select patients for treatment based on the presence of positive PD-L1 expression. Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Hepatocellular cancer: 200 mg IV over 30 minutes every 3 weeks. Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Merkel cell carcinoma: 200 mg IV over 30 minutes every 3 weeks for adult patients and 2 mg/kg IV every 3 weeks for pediatrics (up to 200 mg). Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.
- Renal cell carcinoma: 200 mg IV over 30 minutes every 3 weeks with axitinib 5 mg orally twice daily. Continue treatment until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

Note: For members ≤ 50 kg, a dose of 2 mg/kg every 3 weeks may be used. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be taken into account.

Dose Adjustments

- Withhold pembrolizumab for any of the following (Grades per Common Terminology Criteria for Adverse Events)::
    - Grade 2 pneumonitis
    - Grade 2 or 3 colitis
    - Grade 3 or 4 endocrinopathies
    - Grade 4 hematological toxicity in cHL patients
    - Grade 2 or 3 hypophysitis
    - Grade 3 hyperthyroidism
    - Grade 2 nephritis

    - Grade 3 severe skin reactions or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)
    - Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than 3 and up to 5 times the upper limit of normal (ULN) or total bilirubin greater than 1.5 and up to 3 times the ULN
    - Any other severe Grade 3 treatment-related adverse reaction
- Resume pembrolizumab in patients whose adverse reactions recover to Grade 0-1.
- Permanently discontinue pembrolizumab for any of the following:
    - Any life-threatening adverse reaction (excluding endocrinopathies controlled with hormone replacement therapy, or hematological toxicity in patients with cHL)
    - Grade 3 or 4 pneumonitis or recurrent pneumonitis of Grade 2 severity
    - Grade 3 or 4 hypophysitis
    - Grade 3 or 4 hyperthyroidism
    - Grade 3 or 4 nephritis
    - Grade 4 severe skin reactions or confirmed Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)
    - AST or ALT greater than 5 times the ULN or total bilirubin greater than 3 times the ULN (for patients with liver metastasis, see prescribing information)
    - Grade 3 or 4 infusion-related reactions
    - Inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks
    - Persistent Grade 2 or 3 adverse reactions (excluding endocrinopathies controlled with hormone replacement therapy) that do not recover to Grade 0-1 within 12 weeks after the last dose of pembrolizumab
    - Any severe or Grade 3 treatment-related adverse reaction that recurs

Drug Availability

- 50 mg, lyophilized powder in single-use vial for reconstitution
- 100 mg/4 mL (25 mg/mL) solution in a single-use vial

PRECAUTIONS:

Boxed Warning

None

Contraindications

None

Precautions/Warnings

- Immune-mediated adverse reactions: administer corticosteroids based on the severity of the reaction. See prescribing information for dose modifications and monitoring recommendations for immune-mediated reactions including: pneumonitis, colitis, hepatitis, endocrinopathies (hypophysitis, thyroid disorders, type 1 diabetes mellitus) nephritis, skin reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis).

- Infusion-related reactions: stop infusion and permanently discontinue for severe or life-threatening reactions.
- Embryo-fetal toxicity: May cause fetal harm.
- Multiple myeloma: treatment in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.
- Transplant recipients: Consider the risk of possible organ rejection in donor organ recipients. Also, complications of allogeneic HSCT may occur: Monitor for hepatic veno-occlusive disease, grade 3-4 acute GVHD including hyperacute GVHD, steroid-requiring febrile syndrome, and other immune-mediated adverse reactions. Transplant-related mortality has occurred.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9271	Injection, pembrolizumab, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

C00.0 – C08.9	Malignant neoplasm of lip, base of tongue, of other and unspecified parts of tongue, gum, floor of mouth, palate, of other and unspecified parts of mouth, parotid and salivary gland.
C09.0 – C10.9	Malignant neoplasm of tonsil and oropharynx
C11.0 – C11.9	Malignant neoplasm of nasopharynx
C12.0 – C14.8	Malignant neoplasm of piriform sinus, hypopharynx and other and ill-defined sites in the lip, oral cavity and pharynx.
C15.3 – C15.9	Malignant neoplasm of esophagus
C16.0 – C16.9	Malignant neoplasm of stomach
C17.0 – C17.9	Malignant neoplasm of small intestine
C18.0 – C18.9	Malignant neoplasm of colon
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.0 - C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C23	Malignant neoplasm of gallbladder
C24.0 – C24.9	Malignant neoplasm of other and unspecified parts of biliary tract
C25.0 – C25.9	Malignant neoplasm of pancreas
C30.0	Malignant neoplasm of nasal cavity
C31.0 – C31.9	Malignant neoplasm of accessory sinuses
C32.0 – C32.9	Malignant neoplasm of larynx
C33	Malignant neoplasm of trachea
C34.00 – C34.02	Malignant neoplasm of unspecified main bronchus
C34.10 – C34.12	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.2	Malignant neoplasm of middle lobe, unspecified bronchus or lung
C34.30 – C34.32	Malignant neoplasm of lower lobe, unspecified bronchus or lung

C34.80 – C34.82	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.90 – C34.92	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C37	Malignant neoplasm of thymus
C38.4	Malignant neoplasm of pleura
C40.00 – C40.92	Malignant neoplasm of bone and articular cartilage of limbs
C41.0 – C41.9	Malignant neoplasm of bone and articular cartilage of other and unspecified sites
C43.0 – C43.9	Malignant melanoma of skin
C4A.0 – C4A.9	Merkel cell carcinoma, unspecified
C44.00	Malignant neoplasm of skin of lip
C44.02	Squamous cell carcinoma of skin of lip
C44.09	Other specified malignant neoplasm of skin of lip
C45.0	Mesotheothlioma of pleura
C48.1 – C48.8	Malignant neoplasm of peritoneum
C51.0 – C51.9	Malignant neoplasm of vulva
C53.0 – C53.9	Malignant neoplasm of cervix uteri
C54.0 – C54.9	Malignant neoplasm of corpus uteri
C55	Malignant neoplasm of uterus, part unspecified
C56.1 – C56.9	Malignant neoplasm of ovary
C57.00 – C57.9	Malignant neoplasm of other and unspecified female genital organs
C60.0 – C60.9	Malignant neoplasm of penis
C61	Malignant neoplasm of prostate
C62.00 – C62.92	Malignant neoplasm of testis
C63.7 – C63.8	Malignant neoplasm of overlapping sites and other male genital organs
C64.1 – C64.9	Malignant neoplasm of kidney, except renal pelvis
C65.1 – C65.9	Malignant neoplasm of renal pelvis
C66.1 – C66.9	Malignant neoplasm of ureter
C67.0 – C67.9	Malignant neoplasm of bladder
C68.0	Malignant neoplasm of urethra
C69.30 – C69.32	Malignant neoplasm of choroid
C69.40 – C69.42	Malignant neoplasm of ciliary body
C69.60 – C69.62	Malignant neoplasm of orbit
C69.90	Malignant neoplasm of unspecified site of unspecified eye
C69.91	Malignant neoplasm of unspecified site of right eye
C69.92	Malignant neoplasm of unspecified site of left eye
C74.00 - C74.92	Malignant neoplasm of adrenal gland
C7A.1	Malignant poorly-differentiated neuroendocrine tumors
C7A.8	Other malignant neuroendocrine tumors
C7B.00 - C7B.04	Secondary carcinoid tumors
C7B.1	Secondary Merkel cell carcinoma
C7B.8	Other secondary neuroendocrine tumors
C76.0	Malignant neoplasm of head, face and neck
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C78.00 – C78.89	Secondary malignant neoplasm of respiratory and digestive organs
C79.31	Secondary malignant neoplasm of brain
C79.51 – C79.52	Secondary malignant neoplasm of bone and bone marrow
C79.82	Secondary malignant neoplasm of genital organs

C79.89	Secondary malignant neoplasm of other specified sites
C79.9	Secondary malignant neoplasm of other unspecified site
C80.0	Disseminated malignant neoplasm, unspecified
C80.1	Malignant (primary) neoplasm, unspecified
C81.10 – C81.99	Hodgkin Lymphoma
C82.00 – C82.99	Follicular Lymphoma
C84.00 – C84.19	Mycosis fungoides/Sezary disease
C84.Z0 – C84.Z9	Other mature T/NK-cell lymphomas
C84.90 – C84.99	Mature T/NK-cell lymphomas, unspecified
C85.20 – C85.29	Mediastinal (thymic) large B-cell lymphoma
C86.0	Extranodal NK/T-cell lymphoma, nasal type
D37.01 – D37.9	Neoplasm of uncertain behavior of oral cavity and digestive organs
D38.0	Neoplasm of uncertain behavior of larynx
D38.5	Neoplasm of uncertain behavior of other respiratory organs
D38.6	Neoplasm of uncertain behavior of respiratory organ, unspecified
D39.2 – D39.9	Neoplasm of uncertain behavior of placenta, other female genital organs

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

ALK gene rearrangements – The anaplastic lymphoma kinase (ALK) fusion oncogene is a predictive biomarker that has been identified in a subset of patients with NSCLC. Presence of the ALK arrangement is predictive of treatment benefit with ALK targeted therapies.

EGFR mutation – The presence of the epithelial growth factor receptor (EGFR) mutation (exon 19 deletion or exon 21 L858R mutation) is predictive of treatment benefit from EGFR tyrosine kinase inhibitor therapy

PD-L1 – Cytotoxic T-cell inhibition occurs when binding of the programmed death 1 (PD-1) receptor to one of its ligands: ligand 1 (PD-L1) or 2 (PD-L2). Upregulation of PD-L1 occurs in some tumors and can inhibit active T-cell surveillance of tumors. Presence of the PD-L1 biomarker in tumor cells may be predictive of treatment benefit with PD-1 inhibitors.

RELATED GUIDELINES:

Carboplatin (Paraplatin®) IV, 09-J0000-93
Dabrafenib (Tafinlar®) Capsules, 09-J2000-00
Ipilimumab (Yervoy™) IV, 09-J1000-34
Nivolumab (Opdivo®), 09-J2000-33
Trametinib (Mekinist™) Tablets, 09-J1000-99
Vemurafenib (Zelboraf™), 09-J1000-40

OTHER:

Table 2: Eastern Cooperative Oncology Group (ECOG) Performance Status

Grade	Description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead

Table 3: Karnofsky Performance Status (KPS) (%)

	Score	Description
Able to carry on normal activity and to work; no special care needed.	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his personal needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disabled; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not imminent.
	20	Very sick; hospital admission necessary; active supportive treatment necessary.
	10	Moribund; fatal processes progressing rapidly.
	0	Dead

Table 4: Common Terminology Criteria for Adverse Events v4.0 (CTCAE)

Grade	Description
1	Mild; asymptomatic or mild symptoms; clinical diagnostic observations only; intervention not indicated
2	Moderate; minimal, local or noninvasive intervention indicated; limited age-appropriate instrumental activities of daily living
3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living
4	Life-threatening consequences; urgent intervention indicated
5	Death related to adverse event

TABLE 5: Child-Pugh Score and Classification

	1 point	2 points	3 points
Total bilirubin	< 2	2-3	> 3
Serum albumin	> 3.5	2.8-3.5	< 2.8
INR	> 1.7	1.71-2.20	< 2.20
Ascites	None	Mild	Severe
Hepatic encephalopathy	None	Grade I-II	Grade III-IV
Classification of Result: Class A: 5-6 points Class B: 7-9 points Class C: 10-15 points			

REFERENCES:

1. AHFS Drug Information. Bethesda (MD): American Society of Health-System Pharmacists, Inc; 2017 [cited 2017 June 6]. In: STAT!Ref Online Electronic Medical Library [Internet]. Available from: http://online.statref.com/.
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2019 [cited 2019 Mar 25]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2017 - [cited 2017 June 6]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2019 Mar 25]. Available from: http://www.thomsonhc.com/.
5. Keytruda (pembrolizumab) injection [package insert]. Merck Sharp and Dohme Corp. Whitehouse Station, NJ. July 2019.
6. National Cancer Institute. Common Terminology Criteria for Adverse Events. Available at: http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf. Accessed 9/24/15.
7. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019 Anal carcinoma. Available at http://www.nccn.org/professionals/physician_gls/PDF/anal.pdf. Accessed 3/25/19.
8. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). B-cell lymphomas, 2.2019 [cited 2019 Mar 25]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.

9. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Bladder cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/bladder.pdf. Accessed 3/25/19.
10. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Bone cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/bone.pdf. Accessed 3/25/19.
11. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Central nervous system cancers. Available athttp://www.nccn.org/professionals/physician_gls/PDF/cns.pdf. Accessed 3/25/19.
12. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 3.2019. Cervical cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/cervical.pdf. Accessed 3/25/19.
13. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version1.2019. Colon cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf. Accessed 3/25/19.
14. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version1.2019. Esophageal cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/esophageal.pdf. Accessed 3/25/19.
15. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Gastric cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/gastric.pdf. Accessed 3/25/19.
16. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Gestational Trophoblastic Neoplasia (GTN). Available at http://www.nccn.org/professionals/physician_gls/PDF/gtn.pdf. Accessed 3/25/19.
17. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Head and Neck Cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/head-and-neck.pdf. Accessed 3/25/19.
18. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Hepatobiliary Cancers, v. 2.2019]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed 3/25/19.
19. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 3.2018. Hodgkin Lymphoma. Available at http://www.nccn.org/professionals/physician_gls/PDF/hodgkins.pdf. Accessed 3/25/19.
20. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2020. Kidney Cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/kidney.pdf Accessed 06/12/19
21. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Malignant Pleural Mesothelioma. Available at http://www.nccn.org/professionals/physician_gls/PDF/mpm.pdf. Accessed 3/25/19.
22. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 2.2019. Cutaneous Melanoma. Available at http://www.nccn.org/professionals/physician_gls/PDF/melanoma.pdf. Accessed 3/25/19.
23. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 2.2019. Merkel Cell Carcinoma. Available at http://www.nccn.org/professionals/physician_gls/PDF/mcc.pdf. Accessed 3/25/19.
24. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Neuroendocrine and Adrenal Tumors. Available at http://www.nccn.org/professionals/physician_gls/PDF/neuroendocrine.pdf. Accessed 3/25/19.

25. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 3.2019. Non-small cell lung cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/nscl.pdf. Accessed 3/25/19.
26. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Ovarian Cancer, 1.2019 [cited 2019 Mar 25]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
27. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Pancreatic adenocarcinoma. Available at http://www.nccn.org/professionals/physician_gls/PDF/pancreatic.pdf. Accessed 3/25/19.
28. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Penile cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/penile.pdf. Accessed 3/25/19.
29. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 2.2019. Primary Cutaneous Lymphomas. Available at http://www.nccn.org/professionals/physician_gls/PDF/melanoma.pdf. Accessed 3/25/19.
30. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Prostate cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/prostate.pdf. Accessed 3/25/19.
31. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Rectal cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/rectal.pdf. Accessed 3/25/19.
32. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2019. Small cell lung cancer. Available at http://www.nccn.org/professionals/physician_gls/PDF/sclc.pdf. Accessed 3/25/19.
33. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 2.2019. T-cell Lymphomas. Available at http://www.nccn.org/professionals/physician_gls/PDF/t-cell.pdf. Accessed 3/25/19.
34. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Testicular Cancer, 1.2019. [cited 2019 Mar 25]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
35. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 2.2019. Thymomas and thymic carcinomas. Available at http://www.nccn.org/professionals/physician_gls/PDF/thymic.pdf. Accessed 3/25/19.
36. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 3.2019. Uterine neoplasms. Available at http://www.nccn.org/professionals/physician_gls/PDF/uterine.pdf. Accessed 3/25/19.
37. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Version 1.2018. Uveal melanoma. Available at http://www.nccn.org/professionals/physician_gls/PDF/uveal.pdf. Accessed 3/25/19.
38. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology. Vulvar cancer. Version 2.2019. Available at http://www.nccn.org/professionals/physician_gls/PDF/vulvar.pdf. Accessed 3/25/19.
39. National Comprehensive Cancer Network (NCCN). Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network;2019 [cited 2019 Aug 15]. Available from: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.
40. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2019 [2019 Mar 25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 04/10/19.

GUIDELINE UPDATE INFORMATION:

11/15/14	New Medical Coverage Guideline.
06/15/15	Revision to guidelines; consisting of description and position statement and references
07/15/15	Revision to guidelines; updated HCPCS codes
08/15/15	Revision to guidelines; consisting of position statement.
11/15/15	Revision to guideline; consisting of updating position statement, dosing/administration, warnings/precautions, definitions, coding, and references
12/15/15	Revision to guideline; consisting of updating position statement, description and references.
01/01/16	Annual HCPCS coding update: added code J9271 and deleted codes C9027 and J9999.
6/15/16	Revision to guideline; consisting of updating position statement, description, coding and references.
7/15/16	ICD-10 coding update.
8/15/16	Revision to guideline; consisting of updating position statement and references.
9/15/16	Revision to guideline; consisting of updating description, position statement, dosing, warnings, coding and references.
10/15/16	Revision to guideline; consisting of updating position statement and references.
11/15/16	Revision to guideline; consisting of updating position statement, coding, and references.
12/15/16	Revision to guideline; consisting of updating position statement, description, dosing, coding and references.
02/15/17	Review and revision to guideline; consisting of updating position statement, description, coding and references.
04/15/17	Revision to guideline; consisting of updating position statement and references.
05/15/17	Revision to guideline; consisting of updating the position statement and references.
07/15/17	Review and revision to guideline; consisting of updating position statement, description, dosing, coding and references.
09/15/17	Review and revision to guideline; consisting of updating position statement, description, coding and references.
10/15/17	Revision to guideline; consisting of updating position statement, description, coding and references.
11/15/17	Revision to guideline; consisting of updating position statement, description, coding and references.
12/15/17	Revision to guideline; consisting of updating position statement, description, coding and references.
01/15/18	Revision to guideline; consisting of updating position statement, description, coding and references.
02/15/18	Revision to guideline; consisting of updating position statement, coding and references.
03/15/18	Revision to guideline; consisting of updating position statement, coding and references.
04/15/18	Review and revision to guideline; consisting of updating position statement, description, coding and references
05/15/18	Revision to guideline; consisting of updating position statement, coding and references.
06/15/18	Revision to guideline; consisting of updating position statement, coding and references.

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09/15/19	Revision to guideline; consisting of updating position statement, dosing and references.