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Subject: Nivolumab (Opdivo®)

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DESCRIPTION:

Nivolumab (Opdivo) is a monoclonal antibody that enhances the antitumor response by binding to the programmed death receptor-1 (PD-1) and blocking its interaction with ligand 1 and 2 (PD-L1 and PD-L2). It has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with unresectable or metastatic melanoma, microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, and advanced renal cell carcinoma both as a single agent and in combination with ipilimumab. Nivolumab is FDA-approved as a single agent for the treatment of Classical Hodgkin lymphoma that has relapsed or progressed, recurrent or metastatic squamous cell carcinoma of the head and neck, hepatocellular carcinoma, metastatic non-small cell lung cancer (NSCLC), metastatic small cell lung cancer (SCLC), locally advanced or metastatic urothelial carcinoma, and for the adjuvant treatment of melanoma. Certain indications are approved under accelerated approval based on tumor response rate and durability of response (i.e., CHL, urothelial carcinoma, colorectal cancer, hepatocellular carcinoma, and SCLC). Continued approval for these indications may be contingent upon verification and description of clinical benefit in the confirmatory trials.

The initial safety and efficacy of nivolumab were evaluated in a randomized, open-label phase 3 trial (CheckMate-37) of subjects with unresectable (Stage IIIc) or metastatic (Stage IV) melanoma and disease progression following ipilimumab and, if BRAF V600 mutation–positive, a BRAF inhibitor. Subjects were randomized to receive nivolumab 3 mg/kg every 2 weeks (n=268) or investigator's choice of chemotherapy (n=102), either dacarbazine or carboplatin plus paclitaxel. The primary endpoints were objective response rate (ORR) and overall survival. Efficacy was assessed in a single-arm, noncomparative, preplanned interim analysis in the first 120 patients who received nivolumab in Trial 1 and in whom the minimum duration of follow-up was six months.

At six months, the primary endpoint of ORR in the 120 patients who received nivolumab was 32% (4 complete and 34 partial responses) with 87% having a response duration of 2.6 to more than 10 months. The ORR included patients with and without BRAF V600 mutation-positive disease. Evidence of a clinical benefit outside of tumor response rate has not been established. The median duration of exposure was 5.3 months (range, 1 day to 13.8+ months), with a median of 8 doses (range, 1-31) in nivolumab-treated patients, and was 2 months (range, 1 day to 9.6+ months) in chemotherapy-treated patients. In this ongoing trial, 24% of patients received nivolumab for more than 6 months and 3% of patients received nivolumab for more than 1 year.

Nivolumab was discontinued for adverse reactions in 9% of patients, while 26% of patients receiving nivolumab had a drug delay for an adverse reaction. The most common adverse reaction (reported in at least 20% of patients) was rash.

National Comprehensive Cancer Network (NCCN) Guidelines for Anal cancer, Bladder cancer, Central Nervous System Cancers, Colon and Rectal Cancer, Gestational Trophoblastic Neoplasia, Head and Neck cancer, Hepatobiliary Cancer, Hodgkin's Lymphoma, Kidney Cancer, Malignant pleural mesothelioma, Melanoma, Merkel Cell Carcinoma, Non-Small Cell Lung Cancer, Small Cell Lung Cancer, and uveal melanoma all include recommendations for use of nivolumab.

POSITION STATEMENT:

I. Initiation of nivolumab (Opdivo) **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
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. Nivolumab will be used as a single agent 5. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks
Bladder cancer (also includes cancer of the urethra, upper genitourinary tract, and prostate)	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 or carboplatin) b. Disease progressed within 12 months of neoadjuvant or adjuvant treatment with platinum-based therapy 3. Nivolumab will be used as a single agent

	4. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks
Brain metastasis from metastatic melanoma	When **ALL** of the following are met: 1. Nivolumab is used for the treatment newly diagnosed or recurrent brain metastasis from melanoma 2. Nivolumab will be used as a single agent or in combination with ipilimumab 3. Dose does not exceed the following: a. 3 mg/kg every 2 weeks when used as a single-agent b. 1 mg/kg every 3 weeks for four doses when used in combination with ipilimumab, followed by 3 mg/kg every 2 weeks as a single-agent
Classical Hodgkin's Lymphoma (CHL)	When **ALL** of the following are met: 1. Member has relapsed or refractory disease 2. Nivolumab will be used as monotherapy 3. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 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 nivolumab or pembrolizumab therapy 4. **ONE** of the following a. Used as a single agent or in combination with ipilimumab as subsequent therapy following disease progression with oxaliplatin-, irinotecan- or fluoropyrimidine-based therapy b. Used as a single agent as initial therapy in members who are not candidates for more intensive therapy c. Used as a single agent or in combination with ipilimumab following adjuvant FOLFOX or CapeOX if received within the previous year 5. Dose does not exceed the following: a. 240 mg every 2 weeks or 480 mg every 4 weeks when used as a single agent b. 3 mg/kg every 3 weeks for four doses when used in combination with ipilimumab, followed by 240 mg every 2 weeks or 480 mg every 4 weeks as a single-agent

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. Nivolumab will be used as monotherapy 4. Dose does not exceed 240 mg every 2 weeks
Hepatocellular cancer	When **ALL** of the following are met: 1. Member's disease progressed on first line systemic treatment 2. Member's Child-Pugh score is less than or equal to 7 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. Nivolumab will be used as monotherapy 5. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks
Kidney cancer	When **ALL** of the following are met: 1. Member is diagnosed with relapsed or stage IV disease 2. **ONE** of the following:: a. Used in combination with ipilimumab as first-line therapy for member's with predominant clear cell histology b. Used in combination with ipilimumab as first-line therapy for member's with intermediate or poor-risk (see Table 4) c. Used as a single agent or in combination with ipilimumab as subsequent therapy for member's with predominant clear cell histology if not previously used d. Used as a single agent as treatment for member's with non-clear histology 3. Dose does not exceed the following: a. 240 mg every 2 weeks or 480 mg every 4 weeks

	when used as a single agent b. 3 mg/kg every 3 weeks for four doses when used in combination with ipilimumab, followed by either 240 mg every 2 weeks or 480 mg every 4 weeks as a single-agent
Melanoma	When **ONE** of the following are met: A. Treatment of unresectable or metastatic melanoma 1. Nivolumab will be used as a single agent or in combination with ipilimumab 2. Member meets one of the following: a. Nivolumab is used as first-line therapy b. Nivolumab is used as second-line or subsequent therapy for disease progression c. Nivolumab is used as reinduction therapy and ALL of the following: 1. Members disease relapsed or progressed greater than 3 months after initial clinical response or stable disease with previous nivolumab treatment 2. Member does not have any remaining toxicity from previous nivolumab treatment 3. Dose does not exceed the following: a. 240 mg every 2 weeks or 480 mg every 4 weeks when used as a single-agent b. 1 mg/kg every 3 weeks for four doses when used in combination with ipilimumab, followed by either 240 mg every 2 weeks or 480 mg every 4 weeks as a single-agent B. Adjuvant treatment of melanoma 1. **ONE** of the following: a. Member has Stage III disease b. Member had complete lymph node dissection c. Member underwent surgery for disease recurrence and has no evidence of disease following surgery d. Member with metastatic disease who had complete resection with no evidence of disease 2. Nivolumab will be used as a single agent 3. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks
Malignant pleural mesothelioma	When **ALL** of the following are met: 1. Nivolumab will be used as subsequent therapy following

	disease progression with pemetrexed 2. Nivolumab will be used as a single agent or in combination with ipilimumab 3. Dose does not exceed 3 mg/kg every 2 weeks
Merkel cell carcinoma	When **ALL** of the following are met: 1. Member has distant metastatic disease 2. Nivolumab will be used as monotherapy 3. Dose does not exceed 240 every 2 weeks
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 2. **ONE** of the following: a. When used as a single agent and member's disease progressed on or after initial chemotherapy and the member has not previously received a checkpoint inhibitor (e.g., nivolumab, pembrolizumab, or atezolizumab) b. When used as a single agent or in combination with ipilimumab and member has a high tumor mutational burden (i.e., at least 10 mutations per megabase) and has not previously received systemic chemotherapy 3. Member's ECOG performance status is 0-2 4. Dose does not exceed the following: a. 240 mg every 2 weeks or 480 mg every 4 weeks when used as a single agent b. 3 mg/kg every 2 weeks when used in combination with ipilimumab
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. Nivolumab will be used as a single agent or in combination with ipilimumab 4. Dose does not exceed the following: a. 240 mg every 2 weeks when used as a single

	agent b. 1 mg/kg every 3 weeks for four doses when used in combination with ipilimumab, followed by 240 mg every 2 weeks as a single-agent
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. Member's disease progressed on or after platinum-based therapy (e.g., cisplatin or carboplatin) 3. Member's ECOG performance status is 0-3 4. Nivolumab will be used as a single agent 5. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks
Uveal melanoma	When **ALL** of the following are met: 1. Member's disease is unresectable or metastatic 2. Nivolumab will be used as a single agent or in combination with ipilimumab 3. Dose does not exceed the following: a. 3 mg/kg every 2 weeks when used as a single agent b. 1 mg/kg every 3 weeks for four doses when used in combination with ipilimumab, followed by 3 mg/kg every 2 weeks as a single-agent
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. The dose does not exceed the maximum FDA-approved dose

Approval duration: 6 months

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

1. Subsequent treatment of recurrent esophageal cancer
2. Subsequent treatment of recurrent gastric and gastro-esophageal junction cancer
3. Subsequent treatment of relapsed or refractory primary mediastinal B-cell lymphoma

Duration of approval: 6 months

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

1. 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 nivolumab
3. Nivolumab will be continued as a single-agent*
4. Dose does not exceed the following based on indication:
    a. Gestational Trophoblastic Neoplasia, Merkel Cell Carcinoma, and SCLC: 240 mg every 2 weeks
    b. Anal cancer, Bladder cancer, CHL, colon or rectal cancer, hepatocellular cancer, kidney cancer, Melanoma, NSCLC (when used as a single agent), and SCCHN: 240 mg every 2 weeks or 480 mg every 4 weeks
    c. Brain metastasis from metastatic melanoma, malignant pleural mesothelioma, NSCLC (when combined with ipilimumab), and uveal melanoma: 3 mg/kg every 2 weeks
    d. Gastric and gastro-esophageal junction cancer, esophageal cancer, primary mediastinal b-cell lymphoma, and other FDA-approved or NCCN supported diagnosis: does not exceed maximum FDA-approved dosing

Approval duration: 6 months

*Exception for use in combination with ipilimumab for NSCLC and malignant pleural mesothelioma

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

Unresectable or metastatic melanoma:

- Single agent use: 240 mg every 2 weeks or 480 mg every 4 weeks
- In combination with ipilimumab: Administer nivolumab 1 mg/kg as an intravenous infusion over 30 minutes, followed by ipilimumab 3 mg/kg infusion over 90 minutes on the same day, every 3 weeks for 4 doses. The subsequent dose of nivolumab is given as a single agent as 240 mg every 2 weeks or 480 mg every 4 weeks.

Adjuvant treatment of melanoma with lymph node involvement or metastatic disease with complete resection: 240 mg every 2 weeks or 480 mg every 4 weeks.

Metastatic non-small cell lung cancer: 240 mg every 2 weeks or 480 mg every 4 weeks

Metastatic small cell lung cancer: 240 mg every 2 weeks

Advanced renal cell carcinoma and previous use of antiangiogenic therapy: 240 mg every 2 weeks or 480 mg every 4 weeks

Previously untreated patients with intermediate or poor risk advanced renal cell carcinoma in combination with ipilimumab: Administer nivolumab 3 mg/kg intravenous infusion over 30 minutes followed by ipilimumab 1 mg/kg infusion over 30 minutes on the same day every 3 weeks for 4 doses, The subsequent dose of nivolumab is given as a single agent as 240 mg every 2 weeks or 480 mg every 4 weeks.

Classical Hodgkin Lymphoma: 240 mg every 2 weeks or 480 mg every 4 weeks

Recurrent or metastatic squamous cell carcinoma of the head and neck: 240 mg every 2 weeks or 480 mg every 4 weeks

Locally advanced or metastatic urothelial carcinoma: 240 mg every 2 weeks or 480 mg every 4 weeks

Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer:

- Single agent use in adults or pediatric patients 12 years of age and older and 40 kg or more: 240 mg every 2 weeks or 480 mg every 4 weeks
- Single agent use in pediatric patients 12 years of age and older and less than 40 kg: 3 mg/kg every 2 weeks
- In combination with ipilimumab: Administer nivolumab 3 mg/kg as an intravenous infusion over 30 minutes, followed by ipilimumab 1 mg/kg infusion over 30 minutes on the same day, every 3 weeks for 4 doses. The subsequent dose of nivolumab is given as a single agent in adults or pediatric patients 12 years of age and older and 40 kg or more is 240 mg every 2 weeks or 480 mg every 4 weeks. The subsequent dose of nivolumab in pediatric patients 12 years of age and older and less than 40 kg is 3 mg/kg every 2 weeks
- as 240 mg every 2 weeks

Hepatocellular carcinoma: 240 mg every 2 weeks or 480 mg every 4 weeks

Administer as an intravenous infusion over 30 minutes per indication specific dosing until disease progression or unacceptable toxicity.

Note: For members ≤ 67 kg, a dose of 3 mg/kg every 2 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

Refer to prescribing information

Drug Availability

Injection: 40 mg/4 mL,100 mg/10 mL, and 240 mg/24 mL solution in a single-use vial

PRECAUTIONS:

Boxed Warning

None

Contraindications

None

Precautions/Warnings

Immune-mediated adverse reactions: See prescribing information for dose modifications and monitoring recommendations for immune-mediated reactions including: pneumonitis, colitis, hepatitis, endocrinopathies (hypophysitis, adrenal insufficiency, thyroid disorders, hyperglycemia),encephalitis, severe or life-threatening rash, nephritis, renal dysfunction, and infusion reactions.

Infusion reactions: Discontinue for severe and life-threatening infusion reactions. Interrupt or slow the rate of infusion for mild or moderate infusion reactions.

Complications of allogeneic HSCT: Monitor for hyperacute graft-versus-host-disease (GVHD), grade 3-4 acute GVHD, steroid-requiring febrile syndrome, hepatic veno-occlusive disease, and other immune-mediated adverse reactions. Transplant-related mortality has occurred.

Embryofetal toxicity: can cause fetal harm. Advise of potential risk to fetus and use of effective contraception.

Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus desamethasone is not recommended outside of controlled clinical trials

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J9299	Injection, nivolumab, 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
C22.2	Hepatoblastoma
C22.7	Other specified carcinomas of liver
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
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, 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
C38.4	Malignant neoplasm of pleura
D39.2 – D39.9	Neoplasm of uncertain behavior of placenta, other female genital organs
C43.0 – C43.9	Malignant melanoma of skin
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
C4A.0 – C4A.9	Merkel cell carcinoma
C45.0	Mesothelioma of pleura
C61	Malignant neoplasm of prostate (urothelial carcinoma)
C64.1 – C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1 – C65.9	Malignant neoplasm of unspecified renal pelvis
C66.1 – C66.9	Malignant neoplasm of ureter
C67.0 – C67.9	Malignant neoplasm of bladder
C68.0 – C68.9	Malignant neoplasm of other and unspecified urinary organs
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
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
C80.0	Disseminated malignant neoplasm, unspecified
C80.1	Malignant (primary) neoplasm, unspecified
C81.10 – C81.99	Hodgkin Lymphoma
C85.20 – C85.29	Mediastinal (thymic) large B-cell lymphoma
C7B.1	Secondary Merkel cell carcinoma
D37.01	Neoplasm of uncertain behavior of lip
D37.02	Neoplasm of uncertain behavior of tongue
D37.04	Neoplasm of uncertain behavior of the minor salivary glands
D37.05	Neoplasm of uncertain behavior of pharynx
D37.09	Neoplasm of uncertain behavior of other specified sites of the oral cavity
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

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:

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

RELATED GUIDELINES:

Dabrafenib (Tafinlar®) Capsules, 09-J2000-00
Ipilimumab (Yervoy®) Injection, 09-J1000-34
Pembrolizumab (Keytruda®) Injection, 09-J2000-22
Trametinib (Mekinist™) Tablets, 09-J1000-99

OTHER:

TABLE 3: 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			

TABLE 4: International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) Criteria

Prognostic factors	**Notes**
Less than one year from time of diagnosis to systemic therapy	n/a
Karnofsky Performance status <80%	n/a
Hemoglobin < lower limit of normal	Normal: 12 g/dL
Calcium > upper limit of normal	Normal: 8.5 – 10.2 mg/dL
Neutrophil > upper limit of normal	Normal: 2.7 – 7.0 x 10^9/L
Platelets > upper limit of normal	Normal: 150,000 – 400,000
Prognostic risk groups: **Favorable risk:** no prognostic factors **Intermediate risk**: one or two prognostic factors **Poor-risk:** three to six prognostic factors	

TABLE 5: Karnofsky Performance Status (KPS) (%)

Karnofsky Performance Status (KPS) (%)		
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	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

home and care for most personal needs; varying amount of assistance needed.		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

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 07/10/19.

GUIDELINE UPDATE INFORMATION:

04/15/15	New Medical Coverage Guideline.
06/15/15	Revision of guideline; consisting of updating description and position statement and references.
07/1/15	Revision of guideline; consisting of coding update.
08/15/15	Revision of guideline; consisting of position statement, coding.
11/15/15	Revision of guideline; consisting of updating position statement, description, dosing/administration, warnings, 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 J9299 and deleted codes C9453 and J9999.
01/15/16	Revision to guideline; consisting of updating position statement, description, precautions, coding and references.
04/15/16	Review and revision to guidelines; updating position statement, references.
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 position statement, coding and references.
10/15/16	Revision to guideline; consisting of updating position statement, description, precautions, coding and references.
11/15/16	Revision to guideline; consisting of updating position statement, dosing, coding and references.
02/15/17	Review and revision to guideline; updating position statement, description, dosing, coding, and references.
04/15/17	Review and revision to guideline; consisting of updating position statement, description, dosing, coding, and references.
09/15/17	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 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, dosing, 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 and references.
07/15/18	Update to coding.
08/15/18	Revision to guideline; consisting of updating position statement and references.
10/15/18	Revision to guideline; consisting of updating position statement, dosage/administration, and references.
12/15/18	Revision to guideline; consisting of updating position statement, description, coding and references.
05/15/19	Review and revision to guideline; consisting of updating position statement, description, coding and references.
08/15/19	Revision to guideline; consisting of updating position statement , dosing and references.