09-J1000-34

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Subject: Ipilimumab (Yervoy™) Injection

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Position Statement	Dosage/ Administration	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Ipilimumab (Yervoy™), a recombinant, human monoclonal antibody that binds to the cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4), was approved by the US Food and Drug Administration (FDA) in March of 2011 for the treatment of metastatic melanoma. Approval was based on the results of a phase III study of subjects with unresectable metastatic disease that progressed during systemic therapy. Subjects were randomized to one of three arms: ipilimumab plus glycoprotein 100 peptide vaccine (gp100), ipilimumab monotherapy, or gp100 monotherapy. Overall survival was significantly prolonged in both arms treated with ipilimumab when compared to the gp100 alone arm (10 months vs. 6.4 months, $p<0.05$). Additionally, subjects achieved partial response or stable disease after ipilimumab re-induction. In a second phase III study, the efficacy and safety of ipilimumab was evaluated as first-line therapy for metastatic melanoma. Subjects were randomized to dacarbazine plus ipilimumab or dacarbazine plus placebo. Subjected treated with ipilimumab had a longer overall survival when compared with those treated with placebo (11.2 vs. 9.1 months); furthermore, treatment with ipilimumab significantly prolonged the 3-year overall survival when compared to placebo (20.8% vs. 12.2%, HR 0.72, $p<0.01$). Ipilimumab is FDA approved as a single agent for adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy. The FDA has approved ipilimumab in combination with nivolumab for the treatment of unresectable or metastatic melanoma, previously untreated renal cell carcinoma, hepatocellular carcinoma, malignant pleural mesothelioma, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer , and non-small cell lung cancer.

Current National Comprehensive Cancer Network (NCCN) guidelines provide recommendations for the use of ipilimumab for ampullary cancer, bone cancer, colorectal cancer, esophageal cancer,

hepatocellular carcinoma, kidney cancer, melanoma, mesothelioma, non-small cell lung cancer, small bowel adenocarcinoma, and uveal melanoma.

POSITION STATEMENT:

I. Initiation of treatment with ipilimumab (Yervoy™) meets the definition of **medical necessity** when used to treat **EITHER** of the following:

A. Unresectable[†] or metastatic melanoma when **ALL** of the following are met:

1. Member has not received prior therapy with ipilimumab (for members who have received prior ipilimumab therapy as a single agent, refer to criteria for reinduction).
2. Member meets one of the following:
    a. Ipilimumab is used in combination with nivolumab as first-line therapy
    b. Ipilimumab is used as a single agent as second-line or subsequent therapy for disease progression if not previously used
    c. Ipilimumab is used in combination with nivolumab as second-line or subsequent therapy for disease progression if not previously used
    d. Ipilimumab is used in combination with pembrolizumab as second-line or subsequent therapy if not previously used for disease progression on single agent anti-PD-1 therapy
3. The dose does not exceed **ONE** of the following:
    a. 1 mg/kg every 3 weeks for a total of 4 doses when used with nivolumab 3 mg/kg
    b. 3 mg/kg every 3 weeks for a total of 4 doses when used with nivolumab 1 mg/kg
    c. 3 mg/kg every 3 weeks for a total of 4 doses when used as a single agent
    d. 1 mg/kg every 3 weeks for a total of 4 doses when used with pembrolizumab 2 mg/kg

B. Adjuvant treatment of melanoma when **ALL** of the following are met:

1. **ONE** of the following;
    a. Member had complete lymph node dissection
    b. Member underwent surgery for disease recurrence and has no evidence of disease following surgery
    c. Member with metastatic disease who had complete resection with no evidence of disease
2. **ONE** of the following:

a. Ipilimumab will be used as a single agent and the member previously received anti-PD-1 therapy (e.g., nivolumab, pembrolizumab) in the adjuvant setting

b. Ipilimumab will be used in combination with nivolumab

3. The dose does not exceed the following:

a. Single agent: 10 mg/kg every 3 weeks for a total of 4 doses

b. Combination with nivolumab:

i. 3 mg/kg every 3 weeks for a total of 4 doses when used with nivolumab 1 mg/kg

C. Brain metastases from metastatic melanoma when **BOTH** of the following are met:

1. Ipilimumab is used as a single agent or in combination with nivolumab

2. The dose does not exceed the following:

a. Single agent use: 10 mg/kg every 3 weeks for a total of 4 doses

b. In combination with nivolumab: 3 mg/kg every 3 weeks for a total of 4 doses

D. Ampullary cancer when **ALL** of the following are met:

1. Member has metastatic or unresectable disease

2. Tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR]

3. The member has not previously received a checkpoint inhibitor

4. Ipilimumab will be used in combination with nivolumab

5. The dose does not exceed 1 mg/kg every 3 weeks for a total of 4 doses

E. Bone cancer (includes chondrosarcoma, Ewing sarcoma, osteosarcoma, dedifferentiated chondrosarcoma, chordoma, 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 mutational burden-high (TMB-H) with 10 or more mutations per megabase
3. When used as subsequent therapy after disease progression on initial treatment
4. Member has no alternative treatment options
5. Ipilimumab will be used in combination with nivolumab
6. The dose does not exceed 1 mg/kg every 6 weeks

F. Colon or Rectal cancer (includes appendiceal adenocarcinoma) when **ALL** of the following are met:

1. Member has metastatic, unresectable, or T4b disease

2. Tumor is classified as microsatellite instability-high [MSI-H] or mismatch repair deficient [dMMR]
3. The member has not previously received ipilimumab, nivolumab or pembrolizumab therapy
4. Ipilimumab will be used in combination with nivolumab
5. The dose does not exceed 1 mg/kg every 3 weeks for a total of 4 doses

G. Esophageal carcinoma when **ALL** of the following are met:
1. The member has unresectable advanced or metastatic esophageal squamous cell carcinoma
2. Ipilimumab will be used in combination with nivolumab as first line treatment
3. The dose does not exceed 1 mg/kg every 6 weeks

H. Hepatocellular carcinoma 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. Member has not previously been treated with atezolizumab, ipilimumab, nivolumab or pembrolizumab
5. Ipilimumab will be used in combination with nivolumab
6. The dose does not exceed 3 mg/kg every 3 weeks for a total of 4 doses

I. Kidney cancer when **ALL** of the following are met:
1. Member is diagnosed with relapsed or stage IV disease
2. Member meets one of the following:
    a. Ipilimumab is used in combination with nivolumab as first-line therapy for member's with predominant clear cell histology
    b. Ipilimumab is used in combination with nivolumab as first-line therapy for member's with intermediate or poor-risk (see Table 3)

c. Ipilimumab is used in combination with nivolumab as subsequent therapy for member's with predominant clear cell histology if not previously used

3. The dose does not exceed 1 mg/kg every 3 weeks for a total of 4 doses

J. Mesothelioma (includes malignant pleural mesothelioma, malignant peritoneal mesothelioma, pericardial mesothelioma, and tunica vaginalis testis mesothelioma) when **ALL** of the following are met:

1. **ONE** of the following:

a. Ipilimumab will be used as first line therapy

b. Ipilimumab will be used as subsequent therapy if not previously used

2. Ipilimumab will be used in combination with nivolumab

3. The dose does not exceed 1 mg/kg every 6 weeks

K. Non-small cell lung cancer when **ALL** of the following are met:

1. Member's disease is classified as **ONE** of the following:

a. Metastatic

b. Recurrent

c. Advanced

2. **ONE** of the following:

a. First-line therapy for PD-L1 expression ≥ 1% as detected by an FDA-approved test and EGFR and ALK negative

b. First line therapy if no ALK rearrangements, ROS1 rearrangements, EGFR exon 19 deletion, or EGFR p.L858R point mutation in exon 21

c. First line therapy if EGFR and ALK are negative

d. First line therapy for EGFR exon 20 mutation positive tumors

e. First line therapy for KRAS G12C mutation positive tumors

f. First line or subsequent therapy if BRAF V600E mutation is positive

g. First line or subsequent therapy if NTRK1/2/3 gene fusion positive

h. First line or subsequent therapy for MET exon 14 skipping mutation positive tumors

i. First line or subsequent therapy for RET rearrangement positive tumors

j. First line therapy for ERBB2(ERb-B2 Receptor Tyrosine Kinase 2)/HER2 mutation positive tumors

k. Used as subsequent therapy if not previously used after disease progression with targeted therapy for ROS1 rearrangements (e.g., crizotinib, entrectinib,certinib)

l. Used as subsequent therapy if not previously used after disease progression with targeted therapy for ALK rearrangement positive tumors (e.g., crizotinib, certinib, alectinib, brigatinib, lorlatinib)

m. Used as subsequent therapy if not previously used after disease progression with targeted therapy for EGFR exon 19 deletion or EGFR p.L858R point mutation in exon 21 (e.g., afatinib, osimertinib, erlotinib, gefitinib, dacomitinib)

n. Used as subsequent therapy if not previously used after disease progression with targeted therapy for EGFR S768I, L861Q, and/or G719X mutation positive tumors (e.g., afatinib, osimertinib, erlotinib, gefitinib, dacomitinib)

o. When used as maintenance therapy in combination with nivolumab for members who achieved tumor response or stable disease with previous nivolumab/ipilimumab with or without platinum-doublet chemotherapy

3. Ipilimumab is used in combination with nivolumab*

4. The dose does not exceed 1 mg/kg every 6 weeks

L. Small bowel adenocarcinoma

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. Member has not previously received treatment with a checkpoint inhibitor

4. Ipilimumab will be used in combination with nivolumab

5. The dose does not exceed 1 mg/kg every 3 weeks for a total of 4 doses

M. Uveal melanoma when **ALL** of the following are met:

1. Member's disease is unresectable or metastatic

2. Ipilimumab will be used as a single agent or in combination with nivolumab

3. The dose does not exceed 3 mg/kg every 3 weeks for a total of 4 doses

N. Other FDA-approved or NCCN supported diagnosis (not previously listed above)

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: 4 months (16 weeks)

II**. Reinduction** of ipilimumab therapy for treatment of melanoma **meets the definition of medical necessity** when **ALL** of the following criteria are met:

A. Member has completed initial induction therapy (i.e., completed 4 cycles within a continuous 16 week period)

B. Member's disease relapsed or progressed greater than 3 months after initial clinical response or stable disease (i.e., at least 3 months have passed since week 12 of initial cycle)

C. Member did not have severe systemic toxicity with prior ipilimumab use that requires permanent discontinuation as indicated by **ANY** of the following:

1. Any Grade 2 or higher immune-mediated reactions lasting 12 weeks or longer involving any organ system (CTCAE)

2. Inability to reduce corticosteroid to 10 mg prednisone or equivalent per day within 12 weeks of initiation

3. Any Grade 4 or higher immune-mediated reactions involving any organ system (CTCAE)

4. Any recurrent severe Grade 3 or higher immune-mediated reactions requiring systemic immunosuppressive treatment (CTCAE)

5. Any Grade 3 or higher infusion-related reactions (CTCAE)

6. Opthalmologic reactions not improving to grade 1 within 2 weeks of topical therapy or requiring systemic treatment

D. Member does not have any remaining systemic toxicity with prior ipilimumab use

E. The dose does not exceed **ONE** of the following:

1. 1 mg/kg every 3 weeks for a total of 4 doses when used with nivolumab 3 mg/kg

2. 3 mg/kg every 3 weeks for a total of 4 doses when used with nivolumab 1 mg/kg

3. 3 mg/kg every 3 weeks for a total of 4 doses when used as a single agent

4. 1 mg/kg every 3 weeks for a total of 4 doses when used with pembrolizumab 2 mg/kg

Approval duration: 4 months (16 weeks)

III.Continuation of ipilimumab for adjuvant treatment of melanoma, brain metastases due to melanoma, mesothelioma, esophageal squamous cell carcinoma, bone cancer, or non-small cell lung cancer **meets the definition of medical necessity** when the following criteria are met:

A. The member has demonstrated a beneficial response to therapy (e.g., brain mets are stable, no disease recurrence with adjuvant treatment, no disease progression)

B. 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

C. The dose does not exceed the following:

1. Adjuvant treatment of melanoma or brain metastasis (single agent use only): 10 mg/kg every 12 weeks

2. Esophageal squamous cell adenocarcinoma, bone cancer, mesothelioma, or non-small cell lung cancer (in combination with nivolumab): 1 mg/kg every 6 weeks

Approval duration: 1 year

†Includes incomplete resection

*May be combined with or without a platinum and pemetrexed for nonsquamous cell histology or a platinum and paclitaxel for squamous cell histology

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: 3 mg/kg administered intravenously (IV) over 90 minutes every three weeks for a total of 4 doses as a single agent. When combined with nivolumab, 3 mg/kg administered intravenously (IV) over 90 minutes every three weeks for a total of 4 doses. In the event of toxicity, doses may be delayed, but all treatment must be administered within 16 weeks of the first dose.
- Adjuvant treatment of patients with cutaneous melanoma with regional lymph node involvement of more than 1 mm who have undergone complete resection, including lymphadenectomy: 10 mg/kg administered intravenously (IV) over 90 minutes every three weeks for 4 doses followed by 10 mg/kg every 12 weeks for up to 3 years or until documented disease recurrence or unacceptable toxicity. In the event of toxicity, doses are omitted, not delayed.
- Patients with intermediate or poor risk previously untreated advanced renal cell carcinoma in combination with nivolumab: 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, After 4 doses of the combination, nivolumab is given as a single agent as 240 mg every 2 weeks or 480 mg every 4 weeks.

- Treatment of adult and pediatric patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, in combination with nivolumab. 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, After 4 doses of the combination, nivolumab is given as a single agent as 240 mg every 2 weeks.
- Hepatocellular carcinoma following treatment with sorafenib, in combination with nivolumab: 3 mg/kg administered intravenously (IV) over 30 minutes, immediately following nivolumab administered on the same day, every three weeks for a total of 4 doses or until intolerable toxicity or disease progression as a single agent. After 4 doses of the combination, nivolumab is given as a single agent as 240 mg every 2 weeks or 480 mg every 4 weeks.
- Treatment of adults with metastatic non-small cell lung cancer expressing PD-L1 (≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, as first-line treatment in combination with nivolumab: 1 mg/kg administered intravenously (IV) over 30 minutes every 6 weeks with 360 mg every 3 weeks until disease progression, intolerable toxicity or for up to 2 years in patients without disease progression.
- Treatment of adults with metastatic or recurrent non-small cell lung cancer with no EGFR or ALK genomic tumor aberrations as first-line treatment, in combination with nivolumab and 2 cycles of platinum-doublet chemotherapy: 1 mg/kg administered intravenously (IV) over 30 minutes every 6 weeks with nivolumab 360 mg every 3 weeks and histology-based platinum-doublet chemotherapy every 3 weeks for 2 cycles until disease progression, intolerable toxicity or for up to 2 years in patients without disease progression.
- Treatment of adults with unresectable malignant pleural mesothelioma as first-line treatment, in combination with nivolumab: 1 mg/kg administered intravenously (IV) over 30 minutes every 6 weeks with nivolumab 360 mg every 3 weeks until disease progression, intolerable toxicity or for up to 2 years in patients without disease progression.
- Treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma, as first line treatment in combination with nivolumab: 1 mg/kg every 6 weeks with nivolumab 3 mg/kg every 2 weeks or 360 mg every 3 weeks.

Dose Adjustments/Discontinuation

Although dose adjustments are not required for persons with renal impairment or mild hepatic impairment, ipilimumab has not been evaluated in persons with moderate or severe hepatic impairment.

See prescribing information for recommended treatment modifications for immune-mediated adverse reactions.

Ipilimumab should be discontinued for any of the following:

- Grade 2 adverse reactions lasting 6 weeks or longer (CTCAE)
- Inability to reduce corticosteroid dose to 7.5 mg prednisone or equivalent per day
- Grade 3 or 4 adverse reactions (CTCAE)

- Immune-mediated ocular disease that is unresponsive to topical immunosuppressive therapy or requires systemic treatment

Drug Availability: ipilimumab is supplied as a 50 mg/10 mL or 200 mg/40 mL single-use vial.

PRECAUTIONS:

Boxed Warning

- none

Warnings/Precautions

- Immune-mediated adverse reactions: Withhold for severe (grade 3) and permanently discontinue for life-threatening (grade 4) immune-mediated adverse reactions.

  Treatment with ipilimumab can result in severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation. Although the reactions may involve any organ system, the most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis, endocrinopathy, pneumonitis, and nephritis. Evaluate clinical chemistries including liver function, creatinine, adrenocorticotropic hormone (ACTH) level, and thyroid function tests at baseline and before each dose. See prescribing information for dose modifications of immune-mediated reactions.

- Immune-mediated diarrhea or colitis: immune-mediated diarrhea/colitis may be severe or fatal. Cytomegalovirus(CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated diarrhea/colitis.
- Immune-mediated dermatitis: immune-mediated rash or dermatitis, including bullous and exfoliative dermatitis, Stevens Johnson Syndrome and toxic epidermal necrolysis (TEN), may be severe or fatal. Topical emollients and/or topical corticosteroids may be adequate for mild or moderate non-bullous/exfoliative rashes. Withhold or permanently discontinue depending on the severity.
- Immune-mediated hepatitis: Evaluate liver function tests before each dose of ipilimumab. Withhold for moderate and permanently discontinue for severe or life-threatening transaminase or total bilirubin elevation.
- Immune-mediated endocrinopathies: Monitor ACTH level, thyroid function tests and clinical chemistries prior to each dose. Evaluate at each visit for signs and symptoms of endocrinopathy. Institute hormone replacement therapy as needed.
- Immune-mediated pneumonitis: Permanently discontinue for severe or life-threatening pneumonitis. Withhold dose for moderate immune-mediated adverse reactions.
- Immune-mediated nephritis and renal dysfunction: Permanently discontinue for life-threatening serum creatinine elevation. Withhold dose for moderate to severe immune-mediated adverse reactions and monitor changes in renal function.
- Immune-mediated encephalitis: Permanently discontinue for immune-mediated encephalitis. Withhold dose for new onset moderate or severe neurological signs or symptoms.

- 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 allogenic hematopoietic stem cell transplant: Fatal or serious graft-versus-host disease (GVHD) can occur in patients who receive ipilimumab before or after allogeneic hematopoietic stem cell transplantation (HSCT). See prescribing information for more information.
- Embryo-fetal toxicity: Can cause fetal harm. Advise of potential risk to a fetus and use of effective contraception.
- Risks associated with use in combination with nivolumab: additional risks apply to combination use with nivolumab. See prescribing information for more information.

BILLING/CODING INFORMATION:

HCPCS Coding:

J9228	Injection, ipilimumab, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

C15.3 – C15.9	Malignant neoplasm of esophagus
C16.0	Malignant neoplasm of cardia
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
C21.8	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
C24.1	Malignant neoplasm of ampulla of Vater
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
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
C45.0 – C45.9	Mesothelioma of pleura, peritoneum, pericardium, and other sites
C64.1 – C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis

C65.1 – C65.9	Malignant neoplasm of unspecified renal pelvis
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
C72.0 – C72.1	Malignant neoplasm of spinal cord and cauda equina
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
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive 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 Advantage products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

Table 1: 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:

Adoptive Immunotherapy, 01-96400-01

Autologous Bone Marrow and Stem Cell Transplantation, 02-38241-01
Brachytherapy-Oncologic Applications, 04-77260-20
Carboplatin (Paraplatin®) IV, 09-J0000-96
Dermatoscopy, 02-10000-17
Nivolumab (Opdivo), 09-J2000-33
Paclitaxel and Paclitaxel (protein-bound) IV, 09-J1000-05
Positron Emission Tomography (PET Scans) Oncologic Application, 04-78000-17
Proton Beam Therapy, 04-77260-18
Transpupillary Thermotherapy (TTT), 01-92000-20
Whole Body Photography for Early Detection of Malignant Melanoma, 01-96900-03

OTHER:

Table 2: 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 3: 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 109/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 4: Karnofsky Performance Status (KPS) (%)

Karnofsky Performance Status (KPS) (%)		
	100	Normal no complaints; no evidence of disease.

Able to carry on normal activity and to work; no special care needed.	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 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:

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3. Ingenix HCPCS Level II, Expert 2013.
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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 04/08/20.

GUIDELINE UPDATE INFORMATION:

08/15/11	New Pharmacy Coverage Guideline.
01/01/12	Revision to guideline; consisting of updating coding.
02/15/12	Revision to guideline; consisting of modifying position statement and updating coding.
08/15/13	Review and revision to guideline consisting of reformatting and revising description section and position statement; reformatting dosage/administration and precautions section; updating position statement and references.
10/15/14	Review and revision to guideline; consisting of revising the position statement, updating references.
09/15/15	Revision to guideline; consisting of position statement, coding
11/15/15	Review and revision to guideline; consisting of revising position statement;, warnings/precautions section, definitions, coding and references.
12/15/15	Revision to guideline; consisting of updating position statement, description and references.
07/15/16	Review and revision to guideline; consisting of revising position statement, description, dosing, warnings, coding, and references.
09/15/16	Revision to guideline; consisting of updating position statement, description, coding and references.

10/15/16	Revision to guideline; consisting of updating position statement, description, dose adjustments, and references.
04/15/17	Revision to guideline; consisting of updating position statement and references.
09/15/16	Review and revision to guideline; consisting of revising position statement, description, coding, and references.
10/15/17	Revision to guideline; consisting of updating position statement and references.
12/15/17	Revision to guideline; consisting of updating position statement and references.
04/15/18	Review and revision to guideline; consisting of revising position statement, description, coding and references.
05/15/18	Revision to guideline; consisting of updating position statement, coding and references.
08/15/18	Revision to guideline; consisting of updating position statement, coding and references.
12/15/18	Revision to guideline; consisting of updating position statement and references.
05/15/19	Review and revision to guideline; consisting of revising position statement, description, coding and references.
08/15/19	Revision to guideline; consisting of updating position statement and references.
02/15/20	Revision to guideline; consisting of updating the position statement and references.
05/15/20	Review and revision to guideline; consisting of updating the position statement , description, dosing , warnings, and references.
06/15/20	Revision to guideline; consisting of updating the position statement.
07/15/20	Revision to guideline; consisting of updating the position statement, description, dosing, and references.
11/15/20	Revision to guideline; consisting of updating the position statement, description, dosing, and references.
01/15/21	Revision to guideline; consisting of updating the position statement and references.
03/15/21	Revision to guideline; consisting of updating the position statement and references.
12/15/21	Revision to guideline; consisting of updating the position statement and references.
07/15/22	Revision to guideline; consisting of updating the position statement and references.
02/15/23	Revision to guideline; consisting of adding bone cancer to the policy and updating the use the use for adjuvant treatment of melanoma, colon cancer, and non-small cell lung cancer. Updates to description, dosing, coding and references.