This section contains policy related to billing for injection services, listed in alphabetical order by generic drug name or drug type. For general billing policy information regarding injections services, refer to the Chemotherapy: An Overview section in this manual. Additional policy information for chemotherapy drug services can be found in the Chemotherapy: Drugs A-D Policy and Chemotherapy: Drugs P-Z Policy sections in this manual.

Elotuzumab

Elotuzumab is a humanized IgG1 monoclonal antibody that specifically targets the SLAMF7 (signaling lymphocytic activation molecule family member 7) protein. SLAMF7 is expressed on myeloma cells independent of cytogenetic abnormalities. SLAMF7 is also expressed on natural killer cells, plasma cells and at lower levels on specific immune cell subsets of differentiated cells within the hematopoietic lineage.

Elotuzumab directly activates natural killer cells through both the SLAMF7 pathway and Fc receptors. Elotuzumab also targets SLAMF7 on myeloma cells and facilitates the interaction with natural killer cells to mediate the killing of myeloma cells through antibody-dependent cellular cytotoxicity (ADCC).

Indications

Elotuzumab is indicated in combination with lenalidomide and dexamethasone for the treatment of patients ages 18 years or older, with multiple myeloma who have received one to three prior therapies. Pre-medicate with dexamethasone, diphenhydramine, ranitidine and acetaminophen.

Advise patients that lenalidomide has the potential to cause fetal harm.

Authorization

An approved Treatment Authorization Request (TAR) is required for reimbursement. The TAR must state that the treatment is for a patient with multiple myeloma who has received one to three prior therapies.
Required Codes
ICD-10-CM diagnosis code C90.00, C90.01, C90.10 and C90.30

Dosage
10 mg/kg administered intravenously with lenalidomide and dexamethasone:

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Stage of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly</td>
<td>First two cycles</td>
</tr>
<tr>
<td>Every two weeks</td>
<td>Until disease progression or unacceptable toxicity</td>
</tr>
</tbody>
</table>

Billing
HCPCS code J9176 (injection, elotuzumab, 1 mg)

**Emapalumab-lzsg (Gamifant)**
Emapalumab-lzsg is a monoclonal antibody that binds to and neutralizes interferon gamma (IFNγ). Nonclinical data suggests that IFNγ plays a pivotal role in the pathogenesis of hemophagocytic lymphohistiocytosis (HLH) by being hypersected.

**Indications**
All FDA-approved indications

**Dosage**
FDA-approved dosages
TAR Requirement
An approved Treatment Authorization Request (TAR) is required for reimbursement. Medically necessary for the treatment of adult and pediatric (newborn and older) patients with primary HLH when the following criteria are met:

- FDA-approved indications and dosages
- The patient meets the diagnosis criteria of primary HLH
- Refractory, recurrent or progressive disease or intolerance with conventional HLH therapy
- The patient has evidence of active disease as assessed by the treating physician; and
- The patient does not have active infection, including latent tuberculosis (TB)
- The patient will be receiving dexamethasone concurrently with empalumab-lzsg; and
- The patient has not undergone hematopoietic stem cell transplantation (HSCT)

Billing
HCPCS code J9210 (injection, emapalumab-lzsg, 1mg)

Suggested Codes
ICD-10 CM diagnosis code D76.1

Prescribing Restrictions
Frequency of billing = 2 times per week
Maximum billing units = 2,273 mg = 2,273 units
Enfortumab vedotin-ejfv for injection (PADCEV)

Enfortumab vedotin-ejfv is an antibody-drug conjugate (ADC). The antibody is a human IgG1 directed against Nectin-4, an adhesion protein located on the surface of cells. The small molecule, MMAE, is a microtubule-disrupting agent, attached to the antibody via a protease-cleavable linker. Nonclinical data suggest that the anticancer activity of enfortumab vedotin-ejfv is due to the binding of the ADC to Nectin-4-expressing cells, followed by internalization of the ADC-Nectin-4 complex, and the release of MMAE via proteolytic cleavage. Release of MMAE disrupts the microtubule network within the cell, subsequently inducing cell cycle arrest and apoptotic cell death.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

An approved Treatment Authorization Request (TAR) is required for reimbursement.

TAR Criteria

Padcev will be considered medically necessary when all of the following criteria are met:

- Must be prescribed for FDA-approved indications and dosing regimens
- Patient must be 18 years of age or older
- Patient must have a diagnosis of locally advanced or metastatic urothelial cancer
- Failure of both of the following in the neoadjuvant/adjuvant, locally advanced or metastatic setting:
  a. A programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor. Examples of these are avelumab, atezolizumab, durvalumab, nivolumab, and pembrolizumab; and
  b. A platinum-containing chemotherapy (cisplatin or carboplatin based)

Approval duration: six months
Continued Therapy

i. Patient continues to meet initial approval criteria
ii. Patient is responding positively to therapy with improvement or stabilization of disease
iii. Patient has no unacceptable toxicity such as severe hyperglycemia, severe peripheral neuropathy, thrombosis, pancreatitis, etc.

Reauthorization is for six months

Age Limits

Must be 18 years of age or older

Billing

HCPCS code J9177 (injection, enfortumab vedotin-ejfv, 0.25 mg)

Suggested ICD-10 Diagnosis Codes

C65.1, C65.2, C65.9, C66.1, C66.2, C66.9, C67.0, C67.1, C67.2, C67.3, C67.4, C67.5, C67.6, C67.8, C67.9, C68.0

Prescribing Restrictions

Frequency of billing = 125 mg/500 units on days 1, 8 and 15 of a 28-day cycle
Maximum billing unit(s) = 125 mg/500 units
Epirubicin
Epirubicin is an anthracycline cytotoxic agent. Although it is known that anthracyclines can interfere with a number of biochemical and biological functions within eukaryotic cells, the precise mechanisms of epirubicin’s cytotoxic and/or antiproliferative properties have not been completely elucidated.

Indications
For the treatment of:
- Breast cancer
- Gastric cancer
- Soft tissue sarcomas
- Non-Hodgkin lymphoma

Documentation Requirements
Providers must document in the Remarks field (Box 80)/Additional Claim Information field (Box 19) of the claim, or on an attachment, that the body surface area is in excess of 2.5 m² to justify reimbursement of more than 275 mg. Claims for more than 275 mg without proper documentation will be denied.

Billing
HCPCS code J9178 (injection, epirubicin HCl, 2 mg)

Dosage
The maximum dosage is 275 mg per day.
Eribulin Mesylate

Eribulin mesylate is a synthetic analog of halichondrin B, a product isolated from the marine sponge Halichondria okadai. It is a non-taxane inhibitor of the growth phase of microtubules without affecting the shortening phase and sequesters tubulin into nonproductive aggregates. Eribulin exerts its effects via a tubulin-based antimitotic mechanism leading to G2/M cell-cycle block, disruption of mitotic spindles and ultimately, apoptotic cell death after prolonged mitotic blockage.

Indications

For the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

Required Codes

ICD-10-CM diagnosis codes C50.011 thru C50.929

Dosage

The recommended dose is 1.4 mg/m2 administered intravenously over two to five minutes on days one and eight of a 21-day cycle. A dose in excess of 3 mg is reimbursable with documentation of body surface area larger than 2 m².

Billing

HCPCS code J9179 (injection, eribulin mesylate, 0.1 mg)

Fam-trastuzumab Deruxtecan-nxki(Enhertu®)

Fam-trastuzumab deruxtecan-nxki is a HER2-directed antibody-drug conjugate. The antibody is a humanized anti-HER2 IgG1. The small molecule, DXd, is a topoisomerase I inhibitor attached to the antibody by a cleavable linker. Following binding to HER2 on tumor cells, fam-trastuzumab deruxtecan-nxki undergoes internalization and intracellular linker cleavage by lysosomal enzymes. Upon release, the membrane-permeable DXd causes damage and apoptotic cell death.

Indications

All FDA-approved indications
Dosage
FDA-approved dosages

TAR Requirement
No Treatment Authorization Request (TAR) is required for reimbursement.

Age Limits
Must be 18 years of age or older

Billing
HCPCS code J9358 (injection, fam-trastuzumab deruxtecan-nxki, 1 mg)

Prescribing Restriction
Frequency of billing = 5.4 mg/kg every three weeks

Filgrastim-aafi
Filgrastim-aafi is a leukocyte growth factor for intravenous (IV) or subcutaneous (SQ) administration. Filgrastim-aafi is biosimilar to filgrastim.

Indications
- Filgrastim-aafi is used to enhance neutrophil production for the following indications:
  - Non-myeloid malignancies in patients receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
  - Acute myeloid leukemia (AML) in patients receiving induction or consolidation chemotherapy.
  - Non-myeloid malignancies in patients receiving myeloablative chemotherapy prior to a bone marrow transplant.
  - Mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis in patients receiving cell therapy.
  - Severe chronic neutropenia in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.
Dosage
The recommended dose of filgrastim-aafi varies depending on the treatment indication.

Age
All ages

Authorization
No Treatment Authorization Request (TAR) is generally required for reimbursement.

Required Codes
One of the following ICD-10-CM diagnosis codes is required for reimbursement:
- D70.0 (Congenital agranulocytosis)
- D70.1 (Agranulocytosis secondary to cancer chemotherapy)
- D70.4 (Cyclic neutropenia)
- D70.8 (Other neutropenia)
- D70.9 (Neutropenia, unspecified)
- Z51.11 (Encounter for antineoplastic chemotherapy)

Billing
HCPCS code Q5110 (injection, filgrastim-aafi, biosimilar [nivestym], 1 mcg)
One (1) unit of Q5110 = 1 microgram of filgrastim-aafi

Fludarabine
Fludarabine phosphate is the fluorinated nucleotide analog of the antiviral agent vidarabine. After metabolization it appears to act by inhibiting DNA polymerase alpha, ribonucleotide reductase and DNA primase, thus inhibiting DNA synthesis. The mechanism of action is not completely characterized and may be multi-faceted.
Indications
Fludarabine may be used in the treatment of any of the following:

- Chronic lymphocytic leukemia
- Waldenstrom’s macroglobulinemia
- Non-Hodgkin lymphoma
- Acute myeloid leukemia

Dosage
The usual dose is 25 mg/m² daily for five consecutive days with each five-day course of treatment commencing every 28 days.

Billing
HCPCS code J9185 (injection, fludarabine phosphate, 50 mg).

Fosnetupitant-Palonosetron
Fosnetupitant-Palonosetron 235 mg/0.25 mg is a combination solution for intravenous (IV) administration. Fosnetupitant is a substance P/neurokinin-1 (NK-1) receptor antagonist, and palonosetron is a serotonin-3 (5-HT3) receptor antagonist.

Indications
Fosnetupitant-Palonosetron 235 mg/0.25 mg is indicated in combination with dexamethasone to prevent acute and delayed nausea and vomiting associated with initial and repeat courses of highly-emetogenic cancer chemotherapy.

Age
18 years and older

Dosage
A single dose of 235 mg fosnetupitant/0.25 mg palonosetron is administered by IV infusion over 30 minutes starting 30 minutes before chemotherapy. Dexamethasone 12 mg should also be administered 30 minutes prior to chemotherapy, followed by dexamethasone 8 mg once daily for three additional days.
Authorization
No Treatment Authorization Request (TAR) is generally required for this service.

Required Codes
The following ICD-10-CM diagnosis code is required for reimbursement:
- Z51.11 (Encounter for antineoplastic chemotherapy)

Billing
HCPCS code J1454 (injection, fosnetupitant 235 mg and palonosetron 0.25 mg)
One (1) unit of J1454 = fosnetupitant 235 mg and palonosetron 0.25 mg

Fulvestrant
Fulvestrant is an estrogen receptor antagonist that binds to the estrogen receptor in a competitive manner with affinity comparable to that of estradiol and downregulates the estrogen receptor protein in human breast cancer cells.

Indications
Fulvestrant is indicated for the treatment of hormone receptor-positive, metastatic breast cancer in postmenopausal women with disease progression following anti-estrogen therapy.

Dosage
The recommended dose is 250 mg, administered intramuscularly into each buttock (for a total dose of 500 mg), on days 1, 15, 29 and once monthly thereafter.

For patients with moderate hepatic impairment, the total dose is reduced to 250 mg, administered into one buttock, on days 1, 15, 29 and once monthly thereafter.

Billing
HCPCS code J9395 (injection, fulvestrant, 25 mg)

Gemcitabine
Gemcitabine is a nucleoside metabolic inhibitor that exhibits anti-tumor activity. It kills cells undergoing DNA synthesis and blocks the progression of cells through the G1/S-phase boundary.
Indications
For the treatment of:
- Gallbladder and extrahepatic bile ducts
- Pancreas
- Bronchus and lung
- Breast
- Ovary and other uterine adnexa
- Bladder
- Lymphatic and hematopoietic tissue

Dosage
The dose varies according to the disease being treated. Please see the appropriate medical literature for specifics.

Billing
HCPCS code J9201 (injection, gemcitabine HCl, 200 mg)
Gemcitabine is reimbursable when billed in conjunction with CPT® code 96413 (chemotherapy administration, intravenous infusion technique; up to one hour, single or initial substance/drug).

Gemcitabine (Infugem)
Infugem is the First Formulation of Premixed, Ready-to-Administer Intravenous Chemotherapy. Gemcitabine kills cells undergoing DNA synthesis and blocks the progression of cells through the G1/S-phase boundary. Gemcitabine is metabolized by nucleoside kinases to diphosphate (dFdCDP) and triphosphate (dFdCTP) nucleosides. Gemcitabine diphosphate inhibits ribonucleotide reductase, an enzyme responsible for catalyzing the reactions that generate deoxynucleoside triphosphates for DNA synthesis, resulting in reductions in deoxynucleotide concentrations, including dCTP. Gemcitabine triphosphate competes with dCTP for incorporation into DNA. The reduction in the intracellular concentration of dCTP by the action of the diphosphate enhances the incorporation of gemcitabine triphosphate into the DNA (self-potentiation). After the gemcitabine nucleotide is incorporated into DNA, only one additional nucleotide is added to the growing DNA strands, which eventually results in the initiation of apoptotic cell death.
**Indications**

All FDA-approved indications

**Dosage**

FDA-approved dosages

**TAR Requirement**

No *Treatment Authorization Request* (TAR) is required for reimbursement.

**Billing**

HCPCS code J9198 (injection, gemcitabine hydrochloride (infugem), 100 mg

**Gemtuzumab Ozogamicin**

Gemtuzumab ozogamicin (Mylotarg™) is an antibody-drug conjugate (ADC) composed of the CD33-directed monoclonal antibody (hP67.6; recombinant humanized immunoglobulin [Ig] G4, kappa antibody produced by mammalian cell culture in NS0 cells) that is covalently linked to the cytotoxic agent N-acetyl gamma calicheamicin.

Gemtuzumab ozogamicin is a CD33-directed antibody-drug conjugate (ADC). The antibody portion (hP67.6) recognizes human CD33 antigen. The small molecule, N-acetyl gamma calicheamicin, is a cytotoxic agent that is covalently attached to the antibody via a linker. Nonclinical data suggest that the anticancer activity of gemtuzumab ozogamicin is due to the binding of the ADC to CD33-expressing tumor cells, followed by internalization of the ADC-CD33 complex, and the intracellular release of N-acetyl gamma calicheamicin dimethyl hydrazide via hydrolytic cleavage of the linker. Activation of N-acetyl gamma calicheamicin dimethyl hydrazide induces double-strand DNA breaks, subsequently inducing cell cycle arrest and apoptotic cell death.

**Indications**

Gemtuzumab ozogamicin is indicated for:

- Treatment of newly diagnosed CD33-positive acute myeloid leukemia (AML) in patients 18 years and older
- Treatment of relapsed or refractory CD33-positive AML in adults and in pediatric patients 2 years and older
Dosage

Newly-diagnosed, de novo AML (combination regimen):
- Induction: 3 mg/m² (up to one 4.5 mg vial) on days one, four and seven in combination with daunorubicin-cytarabine
- Consolidation: 3 mg/m² on day one (up to 4.5 mg vial) in combination with daunorubicin-cytarabine

Newly-diagnosed AML (single-agent regimen):
- Induction: 6 mg/m² on day one and 3 mg/m² on day eight
- Continuation: For patients without evidence of disease progression following induction, up to eight continuation courses of Mylotarg mg/m² on day one every four weeks

Relapsed or refractory AML (single-agent regimen):
- 3 mg/m² on days one, four and seven

Pre-medicate with a corticosteroid, antihistamine and acetaminophen one hour prior to Mylotarg.

Required Codes
ICD-10-CM diagnosis codes C92.00, C92.01, C92.A1, C92.A0 and C92.02

Billing
HCPCS code J9203 (injection, gemtuzumab ozogamicin, 0.1 mg)

Ibritumomab Tiuxetan
For HCPCS codes A9542 and A9453, refer to the Radiology: Oncology section in this manual for information about diagnostic and treatment applications of this radiopharmaceutical injection.

Ifosfamide
Ifosfamide is chemically related to the nitrogen mustards and a synthetic analog of cyclophosphamide.
Indications
For the treatment of:

- Cervical cancer
- Hodgkin lymphoma
- Non-Hodgkin lymphoma
- Non-small cell lung cancer
- Osteogenic sarcoma
- Ovarian cancer
- Small cell lung cancer
- Soft tissue sarcoma
- Testicular cancer
- Uterine cancer

Dosage
Recommended dosages cannot be provided because they vary widely depending on the malignancy being treated. The maximum dose is 15 grams. Increased dose is allowed for more than 15 grams if there is documentation that the patient body surface area is more than 2.0 meters$^2$.

Billing
HCPCS code J9208 (injection, ifosfamide, 1 gm)

Inotuzumab Ozogamicin
Inotuzumab ozogamicin is a CD22-directed antibody-drug conjugate (ADC) for intravenous (I.V.) administration.

Indications
Inotuzumab ozogamicin is used for the treatment of patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Age
18 years and older
Dosage
A full course of inotuzumab ozogamicin consists of a single induction cycle followed by a maximum of 5 consolidation cycles:

- For induction: a dose of 0.8 mg/m$^2$ IV is administered on treatment day #1, followed by a dose of 0.5 mg/m$^2$ on days #8 and 15. The cycle length is 21 days.
- For consolidation: a dose of 0.5 mg/m$^2$ IV is administered on treatment days #1, 8, and 15. The cycle length is 28 days, up to a maximum of 6 consolidation cycles.
- The recommended dose and number of treatment cycles varies based on the patient’s response to treatment and whether or not the patient will proceed to a hematopoietic stem cell transplant (HSCT).

Authorization
An approved Treatment Authorization Request (TAR) is required for reimbursement. The TAR must include clinical documentation that demonstrates the following:

- The service is medically necessary to treat relapsed or refractory B-cell precursor ALL.
- Alternative treatments have been tried or considered, have failed, or are contraindicated.
- The physician’s legible, complete, and signed treatment plan/chemotherapy order for inotuzumab ozogamicin.

Billing
HCPCS code J9229 (injection, inotuzumab ozogamicin, 0.1 mg)
One (1) unit of J9229 = 0.1 mg inotuzumab ozogamicin
**Ipilimumab**

Ipilimumab is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody solution for intravenous (IV) administration.

**Indications**

Ipilimumab is used to treat the following conditions:

- **Colorectal Cancer**
  - Metastatic disease, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), in combination with nivolumab

- **Melanoma**
  - Unresectable or metastatic disease
  - Cutaneous disease with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy, adjuvant treatment

- **Renal Cell Carcinoma**

- **Advanced disease, previously untreated with intermediate or poor risk, in combination with nivolumab**

**Age**

12 years and older

**Dosage**

The recommended dosage varies based on the treatment condition:

- **Colorectal Cancer, metastatic disease:**
  - 1 mg/kg IV every 3 weeks for 4 doses, administered in conjunction with nivolumab

- **Melanoma, unresectable or metastatic disease:**
  - 3 mg/kg IV every 3 weeks for a maximum of 4 doses

- **Melanoma, cutaneous disease, adjuvant treatment:**
  - 10 mg/kg IV every 3 weeks for 4 doses, followed by 10 mg/kg IV every 12 weeks for up to 3 years until disease progresses or unacceptable toxicity occurs

- **Renal Cell Carcinoma, advanced:**
  - 1 mg/kg IV every 3 weeks for 4 doses, administered in conjunction with nivolumab
Authorization

An approved *Treatment Authorization Request* (TAR) is required for reimbursement. The TAR must include clinical documentation that demonstrates the following:

- The service is medically necessary.
- Alternative treatments have been tried or considered, have failed, or are contraindicated.
- The physician’s legible, complete, and signed treatment plan/order for ipilimumab.

Billing

HCPCS code J9228 (injection, ipilimumab, 1 mg)

One (1) unit of J9228 = 1 mg of ipilimumab

**Irinotecan**

Irinotecan is used in the treatment of patients with metastatic cancer of the colon or rectum, small cell lung cancer or cervical cancer.

**Required Codes**

Providers may be reimbursed for irinotecan when billed in conjunction with one of the following ICD-10-CM diagnosis codes:

- C18.0 thru C20
- C34.00 thru C34.92
- C53.0 thru C53.9

**Billing**

HCPCS code J9206 (injection, irinotecan, 20 mg)

CPT codes 96413 and 96415 may be billed in conjunction with irinotecan and are separately reimbursable.

For additional information about billing CPT codes 96413 and 96415, refer to “Intravenous Infusion” in the *Chemotherapy: An Overview* section in this manual.
**Irinotecan Liposome**

Irinotecan liposome is a topoisomerase 1 inhibitor encapsulated in a lipid bilayer vesicle or liposome. Topoisomerase 1 relieves torsional strain in DNA by inducing single-strand breaks. Irinotecan liposome and its active metabolite SN-38 bind reversibly to the topoisomerase 1-DNA complex and prevent re-ligation of the single-strand breaks, leading to exposure time-dependent double-strand DNA damage and cell death.

**Indication**

Irinotecan liposome is indicated, in combination with fluorouracil (5-FU) and leucovorin (LV), for the treatment of patients ages 18 years or older with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy.

Irinotecan liposome is not indicated as a single agent for the treatment of patients with metastatic adenocarcinoma of the pancreas.

**Authorization**

An approved TAR is required for reimbursement. The TAR must state that the treatment is for a patient with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy.

**Dosage**

The recommended dose of irinotecan liposome is 70 mg/m² intravenous infusion over 90 minutes every two weeks, administered prior to LV and 5-FU. The recommended starting dose of irinotecan liposome in patients known to be homozygous for the UGT1A1*28 allele is 50 mg/m² administered by intravenous infusion over 90 minutes.

**Required Codes**

ICD-10-CM diagnosis codes C25.4 and C25.9.

**Billing**

HCPCS code J9205 (injection, irinotecan liposome, 1 mg)
Isatuximab-irfc (Sarclisa®)

Isatuximab-irfc is an IgG1-derived monoclonal antibody that binds to CD38 expressed on the surface of hematopoietic and tumor cells, including multiple myeloma cells. Isatuximab-irfc induces apoptosis of tumor cells and activation of immune effector mechanisms including antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and complement dependent cytotoxicity (CDC). Isatuximab-irfc inhibits the ADP-ribosyl cyclase activity of CD38. Isatuximab-irfc can activate natural killer (NK) cells in the absence of CD38-positive target tumor cells and suppresses CD38-positive T-regulatory cells. The combination of isatuximab-irfc and pomalidomide enhanced ADCC activity and direct tumor cell killing compared to that of isatuximab-irfc alone in vitro, and enhanced antitumor activity compared to the activity of isatuximab-irfc or pomalidomide alone in a human multiple myeloma xenograft model.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

No Treatment Authorization Request (TAR) is required for reimbursement.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code J9227 (injection, isatuximab-irfc, 10 mg)

Suggested ICD-10-CM Diagnosis Codes

C90.00, C90.01, C90.02

Prescribing Restrictions

Frequency of billing = 10 mg/kg every week for 4 weeks followed by every 2 weeks
Ixabepilone
Ixabepilone is covered for patients with malignant neoplasm of the breast; providers must document in the Remarks field (Box 80)/Additional Claim Information field (Box 19) of the claim that one of the following conditions was met:

- In combination with capecitabine for the treatment of metastatic or locally advanced breast cancer after failure of an anthracycline and a taxane; or
- As monotherapy for the treatment of metastatic or locally advanced breast cancer after failure of an anthracycline, taxane and capecitabine

Dosage
The maximum daily dosage is 90 mg unless documentation provided notes that the body surface area is greater than 2.25 m². Claims billed for quantities exceeding the daily limitation require appropriate documentation for payment.

Required Codes
Claims must include an ICD-10-CM diagnosis code in the range of C50.011 thru C50.929.

Billing
HCPCS code J9207 (injection, ixabepilone, 1 mg)

Leucovorin Calcium
Leucovorin is one of several active, chemically reduced derivatives of folic acid. Leucovorin is a mixture of the diastereoisomers of the 5-formyl derivative of tetrahydrofolic acid. The biologically active compound of the mixture is the (−)-l-isomer, known as Citrovorum factor, or (−)-folinic acid.

Administration of leucovorin can counteract the therapeutic and toxic effects of folic acid antagonists such as methotrexate, which act by inhibiting dihydrofolate reductase.

In contrast, leucovorin can enhance the therapeutic and toxic effects of fluoropyrimidines used in cancer therapy, such as 5-fluorouracil. Concurrent administration of leucovorin does not appear to alter the plasma pharmacokinetics of 5-fluorouracil. 5-fluorouracil is metabolized to fluorodeoxyuridylic acid, which binds to and inhibits the enzyme thymidylate synthase (an enzyme important in DNA repair and replication).
Indications
Leucovorin is indicated for:

- Leucovorin calcium rescue is indicated after high dose methotrexate therapy in osteosarcoma.
- Leucovorin calcium is indicated in the treatment of megaloblastic anemias due to folic acid deficiency when oral therapy is not feasible.
- Leucovorin calcium is indicated for use in combination with 5-fluorouracil to prolong survival in the palliative treatment of patients with advanced colorectal cancer.

Required Codes
One of the following ICD-10-CM codes is required for reimbursement:
C18.0 thru C20
C40.00 thru C41.9

Dosage
The recommended dosage varies according to the clinical condition being treated. See the appropriate literature for dosing schedules.
The maximum allowable dose is 400 mg daily. A dose greater than 400 mg will be allowed if documentation shows that the body surface area is greater than 2 m².

Billing
HCPCS code J0640 (injection, leucovorin calcium, up to 50 mg)

Leuprolide Acetate Depot Suspension
Leuprolide acetate, a gonadotropin releasing hormone (GnRH) agonist, acts as a potent inhibitor of gonadotropin secretion when given continuously in therapeutic doses. Animal and human studies indicate that after an initial stimulation, chronic administration of leuprolide acetate results in suppression of testicular and ovarian steroidogenesis.

Indications
For the palliative treatment of advanced prostate cancer.
Dosage
The recommended dosing schedule is as follows:

• 7.5 mg monthly
• 22.5 mg every three months
• 30 mg every four months
• 45 mg every six months

Required Code
ICD-10-CM diagnosis code C61

Billing
HCPCS Code J9217 (Leuprolide acetate [for depot suspension] per 7.5 mg)

Note: This is the only HCPCS code that should be used when billing leuprolide acetate (depot suspension) for prostate cancer treatment.

Leuprolide Acetate Implant
Leuprolide acetate implant is reimbursable when used in the treatment of malignant neoplasm of the prostate (ICD-10-CM diagnosis code C61) for male patients 21 years of age or older. The implant is placed under the skin of the patient’s upper inner arm and must be removed and replaced with a new implant every 12 months.

Billing
HCPCS code J9219 (leuprolide acetate implant, 65 mg)
Reimbursement for code J9219 is limited to once in 12 months.
**Levoleucovorin**

Levoleucovorin is the pharmacologically active isomer of 5 formyl tetrahydrofolic acid. Levoleucovorin does not require reduction by the enzyme dihydrofolate reductase in order to participate in reactions utilizing folates as a source of “onecarbon” moieties. Administration of levoleucovorin can counteract the therapeutic and toxic effects of folic acid antagonists such as methotrexate, which act by inhibiting dihydrofolate reductase.

**Indications**

All FDA-approved indications

**Dosage**

FDA-approved dosages

**TAR Requirement**

No *Treatment Authorization Request* (TAR) is required for reimbursement.

**Age Limits**

Must be 6 years of age or older

**Billing**

HCPCS code J0641 (injection, levoleucovorin, 0.5 mg)

**Lutetium Lu 177 dotatate**

Lutetium Lu 177 dotatate is a radiolabeled somatostatin analog for intravenous (I.V.) infusion.

**Indications**

Lutetium Lu 177 dotatate is reimbursable when used to treat somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.
Age
18 years and older

Dosage
7.4 GBq (200 mCi) given I.V. every 8 weeks for a total of 4 doses.

Authorization
An approved Treatment Authorization Request (TAR) is required for reimbursement. The TAR must include clinical documentation that demonstrates the following:

- The service is medically necessary to treat progressive, advanced/inoperable or metastatic somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumor(s);
- Somatostatin receptors are present on the tumor based on diagnostic imaging such as a Gallium Ga-68 dotatate PET/CT scan or by somatostatin receptor scintigraphy (octreotide scan);
- The physician’s legible, complete, and signed treatment plan/order for Lutetium Lu 177 dotatate I.V. infusion.

Billing
HCPCS code A9513 (Lutetium Lu 177, dotatate, therapeutic, 1 mCi)
One (1) unit of A9513 = 1 mCi of Lutetium Lu 177, dotatate injection solution

Medroxyprogesterone
Medroxyprogesterone acetate is indicated for adjunctive therapy and palliative treatment of inoperable, recurrent and metastatic endometrial carcinoma.

Dosage
If improvement is noted and the disease appears to be stabilized, it may be possible to maintain improvement with as little as 400 mg per month.

Authorization
For doses greater than 1,000 mg per day, an approved Treatment Authorization Request (TAR) is required for reimbursement.

Billing
HCPCS code J1050 (injection, medroxyprogesterone acetate, 1 mg)
Melphalan for injection (Evomela®)
Melphalan is an alkylating agent of the bischloroethylamine type. As a result, its cytotoxicity appears to be related to the extent of its interstrand cross-linking with DNA, probably by binding at the N7 position of guanine. Like other bifunctional alkylating agents, it is active against both resting and rapidly dividing tumor cells.

Indications
All FDA-approved indications

Dosage
FDA-approved dosages

TAR Requirement
An approved Treatment Authorization Request (TAR) is required for reimbursement.

TAR Criteria
Evomela will be considered medically necessary when all of the following criteria are met:

- Must be prescribed for FDA-approved indications and dosing regimens
- Patient must be 18 years of age or older
- Patient is taking this as:
  - A high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation
    - Must document approval of stem cell transplantation and tentative procedure date;
      or
    - ii. A palliative treatment when oral therapy is not appropriate

Approval duration: one month for stem cell transplant and six months for palliative treatment
Continued Therapy
  i. Patient continues to meet initial approval criteria
  ii. Patient is responding positively to therapy with improvement or stabilization of disease
  iii. Patient has no unacceptable toxicity such as anaphylaxis

Reauthorization is for 12 months for palliative treatment

Age Limits
Must be 18 years of age or older

Billing
HCPCS code J9246 (injection, melphalan (evomela), 1 mg)

Melphalan Hydrochloride Injection, Not Otherwise Specified (NOS)
Melphalan is an alkylating agent which is a derivative of mechlorethamine that inhibits DNA and RNA synthesis via formation of carbonium ions; cross-links strands of DNA; acts on both resting and rapidly dividing tumor cells.

Indications
All FDA-approved indications

TAR Requirement
An approved Treatment Authorization Request (TAR) is required for reimbursement

TAR Criteria
Melphalan hydrochloride will be considered medically necessary when all of the following criteria are met:
- Must be prescribed for FDA-approved indications and dosing regimens
- Patient must be 18 years of age or older
- Patient must have a diagnosis of multiple myeloma
- Patient is taking this as palliative treatment
- Patient is unable to take oral therapy

Approval duration is six months
Continued Therapy

I. Patient continues to meet initial approval criteria

II. Patient is responding positively to therapy with improvement or stabilization of disease

III. Patient has no disease progression or unacceptable toxicity

Reauthorization is for 12 months

Age

Must be 18 years of age or older

Billing

HCPCS code J9245 (injection, melphalan hydrochloride, not otherwise specified, 50 mg)

Prescribing Restriction

Frequency of billing = 16 mg/m² every two weeks for four doses, then every four weeks

Methotrexate

Injectable methotrexate is reimbursable when used in the treatment of both malignant and non-malignant diseases.

Dosage

Due to the wide variety of diseases and dosages in which methotrexate is used, a usual, recommended or maximum dose cannot be stated.

Billing

HCPCS code J9260 (methotrexate sodium, 50 mg)
One (1) unit = 50 mg

Note: If less than 50 mg is administered, one unit may be submitted on the claim form.
**Mitomycin (Jelmyto™)**

Jelmyto is for pyelocalyceal use only. Mitomycin inhibits the synthesis of deoxyribonucleic acid (DNA). The guanine and cytosine content correlates with the degree of mitomycin-induced cross-linking. At high concentrations of the drug, cellular RNA and protein synthesis are also suppressed.

**Indications**

All FDA-approved indications.

**Dosage**

All FDA-approved dosages.

**TAR Requirement**

No *Treatment Authorization Request* (TAR) is required for reimbursement.

**Age Limits**

Must be 18 years of age or older.

**Billing**

HCPCS code C9064 (mitomycin pyelocalyceal instillation, 1 mg)

**Suggested ICD-10-CM Diagnosis Codes**

C65.1, C65.2, C65.9.

**Prescribing Restrictions**

Frequency of billing = initially, 60 mg/60 units weekly for six weeks. For those with a complete response 3 months after initiation, may administer a monthly dose of 60 mg/60 units for a maximum of 11 additional doses.

Maximum billing unit(s) = 60 mg/60 units}
Mitoxantrone

Injectable mitoxantrone is a synthetic antineoplastic anthracenedione that intercalates into deoxyribonucleic acid causing crosslinks and strand breaks. It also interferes with ribonucleic acid (RNA) and is a potent inhibitor of topoisomerase II, an enzyme responsible for uncoiling and repairing damaged DNA. It has a cytocidal effect on both proliferating and non-proliferating cultured human cells, suggesting lack of cell cycle phase specificity.

Refer to “mitoxantrone” in the Injections: Drugs I-M Policy section of this manual for the use of mitoxantrone in non-malignant conditions.

Indications

For the treatment of:

- Acute myeloid leukemia
- Hodgkin lymphoma
- Non-Hodgkin lymphoma
- Prostate cancer

Dosage

The recommended dose varies depending on the disease being treated.

The maximum dosage is 38 mg per day.

Billing

HCPCS code J9293 (injection, mitoxantrone HCl, per 5 mg)

Mitoxantrone may be billed in conjunction with CPT code 96413 (chemotherapy administration, intravenous infusion technique; up to one hour, single or initial substance/drug).
Mogamulizumab-kpkc (Poteligeo)

Mogamulizumab-kpkc is a defucosylated, humanized IgG1 kappa monoclonal antibody that binds to CCR4, a G protein-coupled receptor for CC chemokines that is involved in the trafficking of lymphocytes to various organs. Non-clinical in vitro studies demonstrate mogamulizumab-kpkc binding targets a cell for antibody-dependent cellular cytotoxicity (ADCC) resulting in depletion of the target cells. CCR4 is expressed on the surface of some T-cell malignancies and is expressed on regulatory T-cells (Treg) and a subset of Th2 T-cells.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

No Treatment Authorization Request (TAR) is required for reimbursement.

Age Limits

Must be 18 years of age or older

Billing

HCPCS code J9204 (injection, mogamulizumab-kpkc, 1 mg)

Prescribing Restriction(s)

Frequency of billing = Every 28 days (4 doses in the first 28 day-cycle, then 2 doses every 28 days thereafter).

Maximum billing unit(s) = 908 mg/ 908 units
**Moxetumomab pasudotox-tdfk (Lumoxiti)**

Moxetumomab pasudotox is a CD22-directed cytotoxin composed of a recombinant murine immunoglobulin genetically fused to truncated Pseudomonas exotoxin (PE38). Moxetumomab pasudotox binds CD22 on the cell surface of B-cells and is internalized. Moxetumomab pasudotox internalization results in ADP-ribosylation of elongation factor 2, inhibition of protein synthesis, and apoptotic cell death.

**Indications**

All FDA-approved indications

**Dosage**

FDA-approved dosages

**TAR Requirement**

No *Treatment Authorization Request* (TAR) is required for reimbursement.

**Recommendations**

It is recommended that:

- Patient has received at least two prior systemic therapies, including treatment with a purine nucleoside analog
- Patient is greater than or equal to 18 years of age
- Patient has not previously received six or more cycles of treatment with Lumoxiti
- Patient must not have severe renal impairment (CrCl is less than or equal to 29 mL/min)

**Age Limits**

Must be 18 years of age or older

**Billing**

HCPCS code J9313 (injection, moxetumomab pasudotox-tdfk, 0.01 mg)

**Prescribing Restrictions**

Frequency of billing = On days 1, 3 and 5 of each 28-day cycle for six cycles

Maximum Billing units = 9.1 mg = 910 units
Necitumumab

Necitumumab is a recombinant human IgG1 monoclonal antibody that binds to the human epidermal growth factor receptor (EGFR) and blocks the binding of EGFR to its ligands. Expression and activation of EGFR has been correlated with malignant progression, induction of angiogenesis and inhibition of apoptosis. Binding of necitumumab induces EGFR internalization and degradation in vitro.

Indications

Necitumumab is indicated, in combination with gemcitabine and cisplatin, for first-line treatment of patients 18 years of age and older with metastatic squamous non-small cell lung cancer.

Necitumumab is not indicated for treatment of non-squamous non-small cell lung cancer.

Authorization

An approved TAR is required for reimbursement. The TAR must state that the treatment is for a patient with metastatic squamous non-small cell lung cancer.

Dosage

The recommended dose is 800 mg as an intravenous infusion over 60 minutes on days one and eight of each three week cycle.

The maximum dose is 800 mg/day.

Required Codes

ICD-10-CM diagnosis codes C25.4 and C25.9

Billing

HCPCS code J9295 (injection, necitumumab, 1 mg)
**Nelarabine**
Nelarabine is reimbursable for treatment of patients with lymphosarcoma or acute lymphoid leukemia.

**Dosage**
The maximum daily dosage on days one, three and five is 4,050 mg unless documented body surface area (BSA) is greater than 2.7 m$^2$. Treatment may be repeated in 21 days.

**Required Codes**
Nelarabine is reimbursable only when billed in conjunction with ICD-10-CM diagnosis codes C83.50 thru C83.59 or C91.00 thru C91.02.

**Billing**
HCPCS code J9261 (injection, nelarabine, 50 mg)

**Nivolumab**
Nivolumab is a programmed death receptor-1 (PD-1)-blocking antibody solution for intravenous (IV) administration.

**Indications**
Nivolumab is used for the treatment of adult patients with the following:

- **Melanoma**
  - Unresectable or metastatic disease.
  - Cutaneous disease with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, adjuvant treatment.

- **Non-Small Cell Lung Cancer**
  - Metastatic disease with progression on or after platinum-based chemotherapy.

- **Small Cell Lung Cancer**
  - Metastatic disease with progression on or after platinum-based chemotherapy and at least one other line of therapy.
• Renal Cell Carcinoma
  – Advanced disease, previously treated with anti-angiogenic therapy or previously untreated with intermediate or poor risk, in combination with ipilimumab.

• Hodgkin’s Lymphoma
  – Relapsed or with progression after autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin or after three or more lines of systemic therapy that includes autologous HSCT.

• Squamous Cell Carcinoma, Head and Neck
  – Metastatic or recurrent disease with progression on or after platinum-based chemotherapy.

• Urothelial Carcinoma
  – Metastatic or locally advanced disease with progression during or following platinum-containing chemotherapy or progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

• Hepatocellular Carcinoma
  – Metastatic or locally advanced disease with progression or intolerance to sorafenib.

Nivolumab is used for the treatment of adolescent and adult patients with the following:

• Colorectal Cancer
  – Metastatic disease, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) with progression, as a single agent or in combination with ipilimumab.

**Age**

12 years and older

**Dosage**

The recommended dosage varies based on the treatment condition.
Authorization

An approved *Treatment Authorization Request* (TAR) is required for reimbursement. The TAR must include clinical documentation that demonstrates the following:

- The service is medically necessary.
- Alternative treatments have been tried or considered, have failed, or are contraindicated.
- The physician’s legible, complete, and signed treatment plan/order for nivolumab.

Billing

HCPCS code J9299 (injection, nivolumab, 1 mg)

One (1) unit of J9229 = 1 mg of nivolumab

Obinutuzumab

Obinutuzumab is a monoclonal antibody that targets the CD20 antigen expressed on the surface of pre B- and mature B-lymphocytes. Upon binding to CD20, obinutuzumab mediates B-cell lysis through:

- Engagement of immune effector cells
- Directly activating intracellular death signaling pathways, and/or
- Activation of the complement cascade

The immune effector cell mechanisms include antibody-dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis.

Indications

In combination with chlorambucil for the treatment of patients 18 years of age and older with previously untreated chronic lymphocytic leukemia.
Dosage
Recommended dose for six cycles (28-day cycles):
- Day 1, cycle 1: 100 mg
- Day 2, cycle 1: 900 mg
- Days 8 and 15, cycle 1: 1,000 mg
- Day 1, cycles 2 through 6: 1,000 mg
The maximum recommended dose is 1,000 mg per day.

Authorization
An approved Treatment Authorization Request (TAR) is required for reimbursement.

Billing
HCPCS code J9301 (injection, obinutuzumab, 10 mg)

Ofatumumab
Ofatumumab is an IgG1 human monoclonal antibody which binds specifically to both the small and large extracellular loops of the CD20 molecule. The CD20 molecule is expressed on normal B lymphocytes and on B-cells of chronic lymphocytic leukemia. The binding of ofatumumab to the CD20 molecule results in B-cell lysis in vitro. Data suggest that possible mechanisms of cell lysis include complement-dependent cytotoxicity and antibody-dependent, cell-mediated cytotoxicity.

Indications
For the treatment of patients with chronic lymphocytic leukemia refractory to fludarabine and alemtuzumab.

Diagnosis Restrictions
Restricted to ICD-10-CM diagnosis code C91.10 or C91.12.
Dosage
The recommended dose and schedule is 12 doses administered as follows:
- Dose 1: 300 mg initial dose, followed one week later by
- Doses 2 through 8: 2,000 mg weekly for seven doses, followed four weeks later by
- Doses 9 through 12: 2,000 mg every 4 weeks for four doses
The maximum daily dosage on days one, three and five is 4,050 mg unless documented body surface area (BSA) is greater than 2.7 m². Treatment may be repeated in 21 days.

Billing
HCPCS Code J9302 (injection, ofatumumab, 10 mg)
One billing unit = 10 mg

Olaratumab
Olaratumab (Lartruvo™) is a platelet-derived growth factor receptor alpha (PDGFR-α) blocking antibody indicated, in combination with doxorubicin, for the treatment of adult patients with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery.

Indications
Olaratumab is indicated for the treatment of adult patients with STS.

Authorization
An approved Treatment Authorization Request (TAR) is required for reimbursement. The TAR must state that the patient has STS with a histologic subtype for which an anthracycline-containing regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery.
Dosage
Administer olaratumab at 15 mg/kg as an intravenous infusion over 60 minutes on days one and eight of each 21-day cycle until disease progression or unacceptable toxicity.

For the first eight cycles, olaratumab:
- Is administered with doxorubicin. Pre-medicate with diphenhydramine and dexamethasone intravenously prior to Lartruvo on day one of cycle one.
- Is for intravenous infusion only.
- Is not to be administered as an intravenous push or bolus.

Billing
HCPCS code J9285 (injection, olaratumab, 10 mg)

Oxaliplatin
Oxaliplatin is a platinum-based antineoplastic agent.

Indications
Oxaliplatin is indicated in the treatment of advanced colorectal cancer, stage III colon cancer (adjuvant) and gastric cancer.

Dosage
Advanced colorectal cancer: 85 mg/m² every two weeks until disease progression or unacceptable toxicity
Stage III colon cancer (adjuvant): 85 mg/m² every two weeks for a total of six months (12 cycles)
Gastric cancer: 100 mg/m² every two weeks

Required Codes
Oxaliplatin is reimbursable only when billed in conjunction with one of the following ICD-10-CM diagnosis codes: C16.0 thru C16.9 and C18.0 thru C20.

Billing
HCPCS code J9263 (injection, oxaliplatin, 0.5 mg)
Legend
Symbols used in the document above are explained in the following table.

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