Chemotherapy: Drugs E-H Policy

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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* manual section. Additional policy information for chemotherapy drug services can be found in manual sections:

- *Chemotherapy: Drugs A Policy*
- *Chemotherapy: Drugs B Policy*
- *Chemotherapy: Drugs C Policy*
- *Chemotherapy: Drugs D Policy*
- *Chemotherapy: Drugs I-L Policy*
- *Chemotherapy: Drugs M Policy*
- *Chemotherapy: Drugs N-O Policy*
- *Chemotherapy: Drugs P-Q Policy*
- *Chemotherapy: Drugs R-S Policy*
- *Chemotherapy: Drugs T-Z Policy.*

Elotuzumab (Empliciti®)

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

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Billing

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

Suggested ICD-10 Diagnosis Codes

C90.00, C90.02, C90.10, C90.12, C90.20, C90.22, C90.30 and C90.32

Elranatamab-bcmm (ELREXFIO™)

Elranatamab-bcmm is a bispecific B-cell maturation antigen (BCMA)-directed T-cell engaging antibody that binds BCMA on plasma cells, plasmablasts, and multiple myeloma cells and CD3 on T-cells leading to cytolysis of the BCMA-expressing cells. Elranatamab-bcmm activated T-cells, caused proinflammatory cytokine release, and resulted in multiple myeloma cell lysis.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

ELREXFIO REMS

ELREXFIO is available only through a restricted program under a REMS called the ELREXFIO REMS because of the risks of CRS and neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

Notable requirements of the ELREXFIO REMS include the following:

- Prescribers must be certified with the program by enrolling and completing training.
- Prescribers must counsel patients receiving ELREXFIO about the risk of CRS and neurologic toxicity, including ICANS, and provide patients with ELREXFIO Patient Wallet Card.
- Pharmacies and healthcare settings that dispense ELREXFIO must be certified with the ELREXFIO REMS program and must verify prescribers are certified through the ELREXFIO REMS program.
- Wholesalers and distributers must only distribute ELREXFIO to certified pharmacies or healthcare settings.

Further information about the ELREXFIO REMS program is available at www.ELREXFIOREMS.com or by telephone at 1-844-923-7845.

Age Limit

Must be 18 years of age or older.

Billing

HCPCS code J1323 (injection, elranatamab-bcmm, 1 mg).

Suggested ICD-10-CM Diagnosis Codes

C90.00, C90.02

Prescribing Restrictions

Maximum billing units equals 76 mg/76 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 is for 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 Limit

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 equals125 mg/500 units on days 1, 8 and 15 of a 28-day cycle.

Maximum billing unit(s) equals 125 mg/500 units.

Epcoritamab-bysp (EPKINLY™)

Epcoritamab-bysp is a T-cell engaging bispecific antibody that binds to the CD3 receptor expressed on the surface of T-cells and CD20 expressed on the surface of lymphoma cells and healthy B-lineage cells.

In vitro, epcoritamab-bysp activated T-cells, caused the release of proinflammatory cytokines, and induced lysis of B-cells.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Age Limit

Must be 18 years of age or older.

Billing

HCPCS code J9321 (injection, epcoritamab-bysp, 0.16 mg)

Required ICD-10-CM Diagnosis Codes

C83.30 thru C83.39

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 m^2 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/m^2 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 m^2.

Billing

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

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Fam-trastuzumab Deruxtecan-nxki (Enhertu®)

Fam-trastuzumab deruxtecan-nxki is a HER2-directed antibody-drug conjugate. The antibody is a humanized anti-HER2 IgGI. 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 Limit

Must be 18 years of age or older.

Billing

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

Prescribing Restriction

Frequency of billing equals 5.4 mg/kg every three weeks.

Fludarabine

Fludarabine phosphate is the fluorinated nucleotide analog of the antiviral agent vidabarine. After metabolization it appears to act by inhibiting DNA polymerase alpha, ribonucleodtide 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/m^2 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).

Fosaprepitant

Fosaprepitant is a prodrug of aprepitant and accordingly, its antiemetic effects are attributable to aprepitant. Aprepitant is a selective high-affinity antagonist of human substance P/neurokinin 1 (NK1) receptors. Aprepitant has little or no affinity for serotonin (5-HT3), dopamine, and corticosteroid receptors, the targets of existing therapies for chemotherapy-induced nausea and vomiting (CINV). Aprepitant has been shown in animal models to inhibit emesis induced by cytotoxic chemotherapeutic agents, such as cisplatin, via central actions. Animal and human Positron Emission Tomography (PET) studies with aprepitant have shown that it crosses the blood brain barrier and occupies brain NK1 receptors. Animal and human studies have shown that aprepitant augments the antiemetic activity of the 5-HT3-receptor antagonist ondansetron and the corticosteroid dexamethasone and inhibits both the acute and delayed phases of cisplatin-induced emesis.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Age Limit

Must be 18 years of age or older.

Billing

HCPCS codes:

J1453 (injection, fosaprepitant, 1 mg).

J1456 (injection, fosaprepitant [teva], not therapeutically equivalent to J1453, 1 mg).

Prescribing Restriction(s)

Frequency of billing: 150 mg/150 units for one dose 30 minutes prior to chemotherapy.

Maximum billing units: 150 mg/150 units.

Fosaprepitant (FOCINVEZ)

Fosaprepitant is a prodrug of aprepitant and accordingly, its antiemetic effects are attributable to aprepitant.

Aprepitant is a selective high-affinity antagonist of human substance P/neurokinin 1 (NK1) receptors. Aprepitant has little or no affinity for serotonin (5-HT3), dopamine and corticosteroid receptors, the targets of existing therapies for chemotherapy-induced nausea and vomiting (CINV). Aprepitant has been shown in animal models to inhibit emesis induced by cytotoxic chemotherapeutic agents, such as cisplatin, via central actions. Animal and human Positron Emission Tomography (PET) studies with aprepitant have shown that it crosses the blood brain barrier and occupies brain NK1 receptors. Animal and human studies have shown that aprepitant augments the antiemetic activity of the 5-HT3-receptor antagonist ondansetron and the corticosteroid dexamethasone and inhibits both the acute and delayed phases of cisplatin-induced emesis.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

TAR Criteria

Focinvez is considered medically necessary when all of the following criteria are met:

- Must be used for FDA-approved indications and dosages.
- Patient must be six months of age or older.

- Focinvez is being used under one of the following conditions (A or B below):

  A. Prevention of Nausea and Vomiting Associated with highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin (for example, Anthracycline/cyclophosphamide combination, Carmustine, Cisplatin, Cyclophosphamide greater than or equal to 1500 mg/m2, Dacarbazine, Mechlorethamine, Streptozocin, etc.).

  B. Prevention of Nausea and Vomiting Associated with moderately emetogenic cancer chemotherapy (MEC) (for example, Alemtuzumab, Arsenic trioxide, Azacitidine, Bendamustine, Busulfan, Carboplatin, Clofarabine, Cyclophosphamide less than 1500 mg/m2, Cytarabine greater than 1000 mg/m2, Daunorubicin, Daunorubicin and cytarabine liposome, Doxorubicin, Epirubicin, Fam-trastuzumab deruxtecan-nxki, Idarubicin, Ifosfamide, Irinotecan, Irinotecan liposomal injection, Oxaliplatin, Romidepsin, Temozolomide,Thiotepa, Trabectedin, etc.).

- Must be used in combination with a 5-HT3 antagonist (for example, ondansetron, palonosetron, granisetron, etc.).
- Must be used in combination with a corticosteroid (for example, dexamethasone as applicable).
- Must use generic fosaprepitant unless intolerant, contraindicated or clinically inappropriate.
- Patient is not taking pimozide.
- Focinvez is not being used for established nausea and vomiting.

Initial approval is for six months.

Reauthorization:

- Patient continues to meet initial approval criteria.
- Patient has documented positive clinical response.
- Patient has absence of unacceptable toxicity from the drug such as severe hypersensitivity reactions, severe infusion site reactions, etc.

Reauthorization is for six months.

Billing

HCPCS code: J1434 (injection, fosaprepitant [focinvez], 1 mg).

Prescribing Restrictions

Frequency of billing equals 150 mg/150 units for one dose 30 minutes prior to chemotherapy.

Maximum billing units equals 150 mg/150 units.

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 Limit

Must be 18 years of age 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 equals 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

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Age Limit

Must be 18 years of age or older (Teva and Fresenius Kabi). No age restrictions on HCPCS code J9395.

Billing

HCPCS code:

J9395 (injection, fulvestrant, 25 mg).

J9393 (injection, fulvestrant [teva] not therapeutically equivalent to J9395, 25 mg).

J9394 (injection, fulvestrant [fresenius kabi] not therapeutically equivalent to J9395, 25 mg).

Gemcitabine

Gemcitabine is a pyrimidine antimetabolite that inhibits DNA synthesis by inhibition of DNA polymerase and ribonucleotide reductase, cell cycle-specific for the S-phase of the cycle (also blocks cellular progression at G1/S-phase). Gemcitabine is phosphorylated intracellularly by deoxycytidine kinase to gemcitabine monophosphate, which is further phosphorylated to active metabolites gemcitabine diphosphate and gemcitabine triphosphate. Gemcitabine diphosphate inhibits DNA synthesis by inhibiting ribonucleotide reductase; gemcitabine triphosphate incorporates into DNA and inhibits DNA polymerase.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Billing

HCPCS codes:

- J9201 (injection, gemcitabine HCl, 200 mg).
- J9196 (injection, gemcitabine hydrochloride [accord], not therapeutically equivalent to J9201, 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 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

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Billing

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

Required Codes

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

Glofitamab-gxbm (COLUMVI)

Glofitamab-gxbm is a bispecific antibody that binds to CD20 expressed on the surface of B cells, and to CD3 receptor expressed on the surface of T cells. Glofitamab-gxbm causes T-cell activation and proliferation, secretion of cytokines, and the lysis of CD20-expressing B cells. Glofitamab-gxbm showed anti-tumor activity in vivo in mouse models of diffuse large B-cell lymphoma (DLBCL).

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Age Limit

Must be 18 years of age or older.

Billing

HCPCS code J9286, (Injection, glofitamab-gxbm, 2.5 mg).

Required ICD-10-CM Diagnosis Codes

C83.30 thru C83.39

Legend

Symbols used in the document above are explained in the following table.

Symbol	Description
‹‹	This is a change mark symbol. It is used to indicate where on the page the most recent change begins.
››	This is a change mark symbol. It is used to indicate where on the page the most recent change ends.