Chemotherapy: Drugs A 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 B Policy
- Chemotherapy: Drugs C Policy
- Chemotherapy: Drugs D Policy
- Chemotherapy: Drugs E-H 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.

Ado-Trastuzumab Emtansine

Ado-trastuzumab emtansine is a Human Epidermal Growth Factor Receptor 2 (HER2)-targeted antibody-drug conjugate which contains the humanized anti-HER2 IgG1, trastuzumab, covalently linked to the microtubule inhibitory drug DM1 (a maytansine derivative) via the stable thioether linker MCC (4-[N- maleimidomethyl] cyclohexane-1-carboxylate). Emtansine refers to the MCC- DM1 complex. Upon binding to sub-domain IV of the HER2 receptor, ado- trastuzumab emtansine undergoes receptor-mediated internalization and subsequent lysosomal degradation, resulting in intracellular release of DM1-containing cytotoxic catabolites. Binding of DM1 to tubulin disrupts microtubule networks in the cell, which results in cell cycle arrest and apoptotic cell death.

Indications

For the treatment of patients with HER2 positive metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. They should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy.

Authorization

An approved *Treatment Authorization Request* (TAR) is required for reimbursement. Documentation must be submitted with the TAR to establish medical necessity.

Dosage

The recommended dose of ado-trastuzumab emtansine is 3.6 mg/kg given as an intravenous infusion every three weeks (21-day cycle) until disease progression or unacceptable toxicity. Ado-trastuzumab emtansine should not be administered at doses greater than 3.6 mg/kg nor should it be substituted for or used with trastuzumab.

Billing

HCPCS code J9354 (injection, ado-trastuzumab emtansine, 1 mg).

Aldesleukin

Aldesleukin is a lymphokine that stimulates growth of T-lymphocytes. Aldesleukin is used to treat metastatic renal cell carcinoma and metastatic malignant melanoma. It is a “biologic response modifier” that promotes anti-tumor activity mediated through the immune system.

Required Codes

Aldesleukin is reimbursable when billed in conjunction with ICD-10-CM diagnosis codes C43.0 thru C43.9 (malignant melanoma of skin), C64.1 thru C65.9 (malignant neoplasm of kidney and renal pelvis).

Dosage

Adult patients diagnosed with metastatic renal cell carcinoma or metastatic malignant melanoma may be treated with a dosage schedule consisting of two five-day treatment cycles separated by a rest period of nine days. Patients receive a dose of 600,000 IU/kg of aldesleukin administered every eight hours through a 15-minute intravenous infusion, for a total of 14 doses. Following the rest period, the schedule is repeated for another 14 doses, to a maximum of 28 doses per course.

Billing

HCPCS code J9015 (injection, aldesleukin, per single use vial).

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

Amivantamab-vmjw (Rybrevant)

Amivantamab-vmjw is a bispecific antibody that binds to the extracellular domains of epidermal growth factor receptor (EGFR) and mesenchymal-epithelial transition (MET). In in vitro and in vivo studies amivantamab-vmjw was able to disrupt EGFR and MET signaling functions through blocking ligand binding and, in exon 20 insertion mutation models, degradation of EGFR and MET. The presence of EGFR and MET on the surface of tumor cells also allows for targeting of these cells for destruction by immune effector cells, such as natural killer cells and macrophages, through antibody-dependent cellular cytotoxicity (ADCC) and trogocytosis mechanisms, respectively.

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 J9061, (injection, amivantamab-vmjw, 2 mg).

Prescribing Restrictions

Frequency of billing equals 1,400 mg/700 units weekly for four weeks, then every two weeks thereafter. Note that the initial dose is administered as a split infusion in week one on days one and two.

Maximum billing unit(s) equals1,400 mg/700 units.

Aprepitant

Aprepitant injection is a substance P/neurokinin-1 (NK-1) receptor antagonist anti-emetic drug for intravenous (I.V.) administration.

Indications

Aprepitant is used in combination with dexamethasone and a 5-HT3 receptor antagonist to prevent nausea and vomiting symptoms associated with initial and repeat courses of highly-emetic cancer chemotherapy (HEC) or moderately-emetic cancer chemotherapy (MEC).

Age Limit

Must be 18 years of age and older.

Dosage

Single Dose Regimen for HEC:

- 130 mg I.V. given as a single dose approximately 30 minutes before initiation of a chemotherapy cycle.

Multiple Dose Regimen for MEC

- 100 mg I.V. given approximately 30 minutes before initiation of a chemotherapy cycle on day one, followed by an 80 mg aprepitant oral capsule given once daily on days two and three.

Authorization

No *Treatment Authorization Request* (TAR) is generally required for reimbursement unless the claim exceeds the recommended maximum dose or frequency.

Required Codes

The following ICD-10-CM diagnosis code is required for reimbursement:

- Z51.11 (Encounter for anti-neoplastic chemotherapy)

Billing

HCPCS code J0185 (injection, aprepitant, 1 mg).

One (1) unit of J0185 equals 1 mg of aprepitant emulsion.

Arsenic Trioxide

The mechanism of action of arsenic trioxide is not completely understood. Arsenic trioxide causes morphological changes and DNA fragmentation characteristic of apoptosis in NB4 human promyelocytic leukemia cells in vitro.

Indications

For the induction of remission and consolidation in patients 4 years of age and older with acute promyelocytic leukemia (APL) who are refractory to, or have relapsed from, retinoid and anthracycline chemotherapy, and whose APL is characterized by the presence of the (15;17) translocation or PML/RAR alpha gene expression.

Dosage

Recommended induction treatment schedule:

Intravenously at a dose of 0.15 mg/kg daily until bone marrow remission. Total induction dose should not exceed 60 doses.

Recommended consolidation treatment schedule:

Intravenously at a dose of 0.15 mg/kg daily for 25 doses over a period of five weeks.

Required Codes

Arsenic trioxide is reimbursable when billed with one of the following ICD-10-CM diagnosis codes: C92.40, C92.41, C92.42

Billing

HCPCS code J9017 (injection, arsenic trioxide, 1 mg).

Asparaginase *Erwinia Chrysanthemi*

Asparaginase *Erwinia chrysanthemi* contains an asparaginase specific enzyme derived from *Erwinia chrysanthemi*. Asparaginase *Erwinia chrysanthemi* catalyzes the deamidation of asparagine to aspartic acid and ammonia, resulting in a reduction in circulating levels of asparagine. The mechanism of action of asparaginase *Erwinia chrysanthemi* is thought to be based on the inability of leukemic cells to synthesize asparagine due to lack of asparagine synthetase activity, resulting in cytotoxicity specific for leukemic cells that depend on an exogenous source of the amino acid asparagine for their protein metabolism and survival.

Indications

For the treatment of patients with acute lymphoblastic leukemia who have developed hypersensitivity to *E. coli*-derived asparaginase.

Dosage

To substitute for a dose of pegaspargase:

The recommended dose is 25,000 International Units/m^2 administered intramuscularly three times a week (Monday/Wednesday/Friday) for six doses for each planned dose of pegaspargase.

To substitute for a dose of native *E. coli* asparaginase:

The recommended dose is 25,000 International Units/m^2 administered intramuscularly for each scheduled dose of native *E. coli* asparaginase within a treatment.

Maximum dose of 50,000 units unless there is documentation that patient‘s body surface area (BSA) is greater than 2.6 m^2.

Required Codes

Asparaginase *Erwinia chrysanthemi* is reimbursable when billed with one of the following ICD-10-CM diagnosis codes: C91.00 or C91.02

Billing

HCPCS code J9019 (injection asparaginase [erwinaze], 1,000 IU)

Asparaginase Erwinia Chrysanthemi (recombinant) Rywn (Rylaze™)

Asparaginase erwinia chrysanthemi (recombinant)-rywn is an enzyme that catalyzes the conversion of the amino acid L-asparagine into aspartic acid and ammonia. The pharmacological effect of Rylaze is based on the killing of leukemic cells due to depletion of plasma asparagine. Leukemic cells with low expression of asparagine synthetase have a reduced ability to synthesize asparagine, and therefore depend on an exogenous source of asparagine for survival.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Billing

HCPCS code J9021, (injection, asparaginase, recombinant, [Rylaze], 0.1 mg).

Suggested ICD-10-CM Diagnosis Codes

C91.00, C91.01, C91.02

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Atezolizumab (Tecentriq®)

Atezolizumab is a humanized monoclonal antibody immune checkpoint inhibitor that binds to programmed death ligand 1 (PD-L1) to selectively prevent the interaction between the programmed cell death-1 (PD-1) and B7.1 (also known as CD80) receptors, while still allowing interaction between PD-L2 and PD-1. PD-L1 is an immune checkpoint protein expressed on tumor cells and tumor infiltrating cells and down regulates anti-tumor t-cell function by binding to PD-1 and B7.1; blocking PD-1 and B7.1 interactions restores antitumor t-cell function. Immune checkpoint inhibition combined with the mitogen-activated protein kinase (MAPK) pathway increase antigen presentation and T-cell infiltration/activation to suppress tumor growth and improve tumor immunogenicity (when compared to targeted therapy alone).

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 J9022 (injection, atezolizumab, 10 mg).

Suggested ICD-10 Diagnosis Codes

Breast Cancer

C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119
C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229
C50.311, C50.312 ,C50.319, C50.321, C50.322, C50.329, C50.411, C50.412, C50.419
C50.421, C50.422, C50.429, C50.511, C50.512, C50.519, C50.521, C50.522, C50.529
C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819
C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929

Hepatocellular Carcinoma

C22.0, C22.1, C22.2, C22.3, C22.4, C22.7, C22.8, C22.9

Lung Cancer

C34.00, C34.01, C34.02, C34.10, C34.11, C34.12, C34.2

Melanoma

C43.0, C43.10, C43.111, C43.112, C43.121, C43.122, C43.20, C43.21, C43.22, C43.30
C43.31, C43.39, C43.4, C43.51, C43.52, C43.59, C43.60, C43.61, C43.62, C43.70, C43.71
C43.72, C43.8, C43.9

Urothelial Carcinoma

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, C67.7, C67.8, C67.9, C68.0

Prescribing Restrictions

Maximum billing unit (s) equals 1680mg/168 units.

Avelumab (Bravencio®)

Avelumab is a programmed death ligand-1 (PD-L1) blocking antibody. PD-L1 may be expressed on tumor cells and tumor-infiltrating immune cells and can contribute to the inhibition of the anti-tumor immune response in the tumor microenvironment. Binding of PD-L1 to the PD-1 and B7.1 receptors found on T cells and antigen presenting cells suppresses cytotoxic T-cell activity, T-cell proliferation and cytokine production. Avelumab binds PD-L1 and blocks the interaction between PD-L1 and its receptors PD-1 and B7.1. This interaction releases the inhibitory effects of PD-L1 on the immune response resulting in the restoration of immune responses, including anti-tumor immune responses.

Indications

FDA approved indications.

Dosage

FDA approved dosages.

Authorization

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

Age Limit

Must be 12 years of age or older.

Billing

HCPCS code J9023 (injection, avelumab, 10 mg)

One (1) unit of J9023 equals 10 mg of avelumab.

Prescribing Restrictions

Frequency of billing equals 800 mg/80 units every two weeks

Maximum billing unit(s) equals 800 mg/80 units.

Axicabtagene ciloleucel (Yescarta®)

YESCARTA, a CD19 (Cluster of Differentiation 19)-directed genetically modified autologous T cell immunotherapy binds to CD19-expressing cancer cells and normal B cells. Studies demonstrated that following anti-CD19 CAR T cell engagement with CD19-expressing target cells, the CD28 and CD3-zeta co stimulatory domains activate downstream signaling cascades that lead to T cell activation, proliferation, acquisition of effector functions and secretion of inflammatory cytokines and chemokines. This sequence of events leads to killing CD19-expressing cells.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

TAR Criteria

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

Universal criteria:

- Must be used for FDA-approved indications and dosages.
- Patient must be 18 years of age or older.
- Must be prescribed by or in consultation with an oncologist or hematologist.
- Patient has an ECOG (Eastern Cooperative Oncology Group) performance status of 0 or 1.
- Patient does not have the following:
  - Primary central nervous system lymphoma
  - Active or serious infection or inflammatory disorders

- Patient must have adequate bone marrow, cardiac, pulmonary, renal hepatic and organ functions.
- Healthcare facility is enrolled in the Yescarta and Tecartus REMS (Risk Evaluation and Mitigation Strategy) Program.
- Outpatient administration is restricted to Hospital Outpatient Services only.
- Patient has not previously received treatment with a CAR T-cell immunotherapy.

A. Relapsed or refractory large B-cell lymphoma:

- Patient must meet the above universal criteria.
- Patient has one of the following histologically proven large B-cell lymphoma as defined by the World Health Organization (WHO) 2016 (Swerdlow et al, 2016).
  - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified [activated B cell (ABC) or germinal center B cell (GCB)]
  - High grade B-cell lymphoma (HGBCL) with or without MYC and BCL2 and/or BCL6 rearrangement
  - DLBCL arising from follicular lymphoma (FL) or Transformation Follicular Lymphoma (TFL)
  - T-cell/histiocyte rich large B-cell lymphoma
  - DLBCL associated with chronic inflammation
  - Primary cutaneous DLBCL, leg type
  - Epstein-Barr virus (EBV) + DLBCL

Treatment is based on 1 or 2 below:

1. Patient had relapsed or refractory disease after first-line chemoimmunotherapy (includes rituximab and anthracycline)
   - Refractory disease defined as no complete remission to first-line therapy.
     - Patient had disease progression after first-line therapy or;
     - Patient had stable disease after at least four cycles of first-line therapy (for example, four cycles of R-CHOP ([rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone]), or
     - Patient had partial response after at least six cycles and biopsy-proven residual disease or disease progression with less than or equal to 12 months of therapy

- Relapsed disease defined as complete remission to first-line therapy followed by biopsy-proven relapse with less than or equal to 12 months of first-line therapy.
- Patient must have received adequate first-line therapy including at a minimum:
  - Anti-CD20 monoclonal antibody (for example, rituximab) unless tumor is CD20 negative, and
  - An anthracycline containing chemotherapy regimen (for example, doxorubicin)
- Patient has not received more than one line of therapy for DLBCL.
- Patient does not have primary mediastinal B-cell lymphoma.
- Patient has not received autologous or allogeneic stem cell transplant.

2. Patient has relapsed or refractory large B-cell lymphoma including DLBCL, PMBCL, TFL and HGBCL after two or more lines of systemic therapy.
   - Therapy includes at a minimum anti-CD20 monoclonal antibody unless the tumor is CD20-negative and an anthracycline containing chemotherapy regimen (for example, doxorubicin).
   - Patient may have primary mediastinal large B-cell lymphoma (PMBCL).
   - Patient had chemotherapy-refractory disease defined as no response to the most recent therapy or relapse within one year after autologous hematopoietic stem cell transplantation (HSCT).
   - Patient did not have prior allogeneic hematopoietic stem cell transplant (HSCT).

<u>B. Relapsed or refractory follicular lymphoma:</u>

- Patient meets the above universal criteria.
- Patient has a histologically confirmed diagnosis of follicular lymphoma.
- Patient has relapsed or refractory disease, defined as progression after two or more lines of systemic therapy (including the combination of an anti-CD20 monoclonal antibody (for example rituximab, obinutuzumab, etc) and an alkylating agent [e.g., R-bendamustine, R-CHOP]).
- Patient does not have transformed lymphoma or other aggressive lymphomas
- Patient did not have prior allogeneic hematopoietic stem cell transplant (HSCT)

Initial approval is for three months (one treatment only).

Reauthorization

Repeat treatment is not approvable.

YESCARTA and TECARTUS REMS:

The goals of the Yescarta and Tecartus REMS are to mitigate the risks of cytokine release syndrome (CRS) and neurological toxicities by:

1. Ensuring that hospitals and their associated clinics that dispense Yescarta and/or Tecartus are specially certified and have on-site, immediate access to tocilizumab.
2. Ensuring those who prescribe, dispense, or administer Yescarta and/or Tecartus are aware of how to manage the risks of CRS and neurological toxicities.

Age Limit

Must be 18 years of age or older.

Billing

HCPCS code Q2041 (Axicabtagene ciloleucel, up to 200 million autologus anti-CD19 CAR T cells, including leukapheresis and dose preparation procedures, per therapeutic dose).

One unit of Q2041 equals a single infusion of up to 200 million autologous anti-CD19 CAR-positive viable T cells.

Administration code: CPT code 96413 (chemo administration, intravenous infusion; up to one hour, single or initial substance or drug).

Important Instructions for Billing

Due to system limitations, providers are to take the following steps when submitting claims for Yescarta:

1. Submit and receive back an approved TAR/Service Authorization Request (SAR)
2. Bill using Q2041 (Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 car-positive viable T cells, including leukapheresis and dose preparation procedures per therapeutic dose).

3. Completion of claim forms:
   - Claims are restricted to hospital outpatient services. Note that claims from pharmacies and clinics will be denied
   - Outpatient claims may be billed by paper claim using *UB-04* or electronically using 837I
   - Providers must submit one service line on the TAR/SAR request and enter “5” in the Units box
   - On the 837I or *UB-04* claim form, providers must submit one claim line to represent one service
     - Claims submitted with more than one claim line will be denied
   - Providers must submit an invoice for reimbursement
   - This process will ensure that the total reimbursement paid for the quantity of five is no more than the paid price on the provider submitted invoice
   - Yescarta must be billed on its own with no other drug or biological
4. For instructions regarding physician claim form completion, refer to the Forms page on the Medi-Cal Providers website for completion of 837I and *UB-04* claim forms.
5. Providers may bill separately for the administration (infusion) of the CAR-T cell using CPT code 96413

Suggested ICD-10-CM Diagnosis Codes

C82.00 thru C82.09, C82.10 thru C82.19, C82.20 thru C82.29, C82.30 thru C82.39, C82.40 thru C82.49, C82.50 thru C82.59, C82.60 thru C82.69, C82.80 thru C82.89, C82.90 thru C82.99, C83.30 thru C83.39, C85.10 thru C85.19, C85.20 thru C85.29, C85.80 thru C85.89.

Prescribing Restrictions

Frequency of billing is once in a lifetime.

Azacitidine

Azacitidine is a pyrimidine nucleoside analog of cytidine and is believed to exert its antineoplastic effects by causing hypomethylation of DNA and direct cytotoxicity on abnormal hematopoietic cells in the bone marrow.

Indications

Azaciditine is indicated for treatment of patients with:

- Refractory anemia
- Refractory anemia with ringed sideroblasts (if accompanied by neutropenia or thrombocytopenia or requiring transfusions)
- Refractory anemia with excess blasts or excess blasts in transformation
- Chronic myelomonocytic leukemia
- Acute myeloid leukemia

Dosage

The recommended starting dosage of azacitidine is 75 mg/m^2, given subcutaneously or intravenously once a day for seven days. This is usually repeated every four weeks for at least four cycles, and then continued as long as the patient continues to improve. The dosage may be increased to a maximum of 100 mg/m^2 if there is no initial response to treatment.

Billing

HCPCS code J9025 (injection, azacitidine, 1 mg)

Azacitidine is reimbursable for either intravenous or subcutaneous administration. Azacitidine may be billed either as an I.V. push or I.V. infusion over 40 minutes.

Note: Refer to the *Chemotherapy: An Overview* section of this manual for both subcutaneous injection and I.V. infusion administration billing codes.

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.