# Injections: Drugs E-H Policy

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This section outlines 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 *Injections: An Overview* section in this manual. Additional policy information for injection services can be found in the following sections of this manual:

- *Injections: Drugs A–D Policy*
- *Injections: Drugs I–M Policy*
- *Injections: Drugs N–R Policy*
- *Injections: Drugs S–Z Policy*
- *Injections: Hydration*
- *Immunizations*

# Ecallantide

Hereditary angioedema (HAE) is a rare genetic disorder caused by mutations to C1-esterase-inhibitor (C1-INH) located on chromosome 11q and inherited as an autosomal dominant trait. HAE is characterized by low levels of C1-INH activity and low levels of C4. C1-INH functions to regulate the activation of the complement and intrinsic coagulation pathways and is a major endogenous inhibitor of plasma kallikrein. The kallikrein-kinin system is a complex proteolytic cascade involved in the initiation of both inflammatory and coagulation pathways. One critical aspect of this pathway is the conversion of High Molecular Weight (HMW) kininogen to bradykinin by the protease plasma kallikrein. In HAE, normal regulation of plasma kallikrein activity and the classical complement cascade is therefore not present. During attacks, unregulated activity of plasma kallikrein results in excessive bradykinin generation. Bradykinin is a vasodilator which is thought by some to be responsible for the characteristic HAE symptoms of localized swelling, inflammation and pain.

Ecallantide is a potent selective, reversible inhibitor of plasma kallikrein that binds to plasma kallikrein and blocks its binding site, inhibiting the conversion of HMW kininogen to bradykinin. By directly inhibiting plasma kallikrein, ecallantide reduces the conversion of HMW kininogen to bradykinin and thereby treats symptoms of the disease during acute episodic attacks of HAE.

## Indications

Ecallantide is indicated for the treatment of acute attacks of hereditary angioedema in patients 12 years of age and older.

## Diagnosis Restrictions

Restricted to ICD-10-CM diagnosis code D84.1.

## Dosage

The recommended dose is 30 mg administered subcutaneously in three 10 mg injections. If the attack persists, an additional dose of 30 mg may be administered within a 24-hour period.

## Billing

HCPCS code J1290 (injection, ecallantide, 1 mg)

One billing unit = 1 mg

# Eculizumab (Soliris®)

Soliris is a monoclonal antibody that inhibits terminal complement activation. It is used for paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), anti-acetylcholine receptor antibody positive generalized myasthenia gravis (gMG), and anti-aquaporin-4 antibody positive neuromyelitis optica spectrum disorder (NMOSD). It is associated with an increased risk of meningococcal infections.

## Indications

All FDA-approved indications

## Dosage

FDA-approved dosages

## TAR Requirement

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

## TAR Criteria

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

- Must be prescribed for FDA-approved indications and dosages
- Prescriber must be enrolled in the Soliris REMS program
- Vaccination against Neisseria meningitides at least two weeks prior to initiation (unless Soliris [eculizumab] treatment cannot be delayed), and
- Patient must have one of the following diagnoses:
  - A diagnosis of Paroxysmal nocturnal hemoglobinuria (PNH)
    - ❖ Documented baseline value for serum lactate dehydrogenase (LDH)
    - ❖ Patient must be 18 years of age or older
    - ❖ Patient is not on another terminal complement inhibitor such as Ultomiris (ravulizumab-cwvz)

- A diagnosis of Atypical hemolytic uremic syndrome (aHUS)
  - Documented baseline value for serum lactate dehydrogenase (LDH)
  - Patient is 2 months of age or older and has a weight of at least five kilograms
  - Patient does not have Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)
  - Patient is not on another terminal complement inhibitor such as Ultomiris (ravulizumab-cwvz)
- A diagnosis of generalized Myasthenia Gravis (gMG)
  - Positive serologic test for anti-acetylcholine antibodies
  - Patient must be 18 years of age or older
  - Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV
  - Documented baseline MG-Activities of Daily Living (MG-ADL) total score ≥ 6
  - Patient has had an inadequate treatment response, intolerance or contraindication to two or more immunosuppressants such as azathioprine, cyclophosphamide, cyclosporine, mycophenolate, tacrolimus, methotrexate, etc.
  - Patient has had an inadequate treatment response, intolerance, or contraindication to chronic IVIG therapy
- A diagnosis of Neuromyelitis optica spectrum disorder (NMOSD)
  - Positive serologic test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG)/NMO-IgG antibodies
  - Patient must be 18 years of age or older

## REMS Program

Eculizumab is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) due to the increased risk of infection and death from the meningococcal disease after administration of eculizumab. Prescribers must enroll in the Soliris REMS program to ensure that patients are counseled about the risk of meningococcal infection and receive appropriate vaccination(s) and/or drug prophylaxis prior to receiving eculizumab. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1888-765-4747) or at www.solirisrems.com.

Initial authorization is for six months

Reauthorization

The patient must have a significant clinical response as evidenced by:

- Paroxysmal nocturnal hemoglobinuria (PNH)
  - Documentation of a reduction in serum LDH from pretreatment baseline
- Atypical hemolytic uremic syndrome (aHUS)
  - Documentation of a reduction in serum LDH from pretreatment baseline
- Myasthenia Gravis (gMG)
  - Documentation of reduction of (MG-ADL) total score from baseline
- Neuromyelitis optica spectrum disorder (NMOSD)
  - Patient has had fewer relapses while on Soliris therapy

Reauthorization is for 12 months

## Age

Must be 2 months or older for aHUS diagnosis

Must be 18 years of age or older for PNH, gMG or NMOSD diagnosis

## Suggested Codes

ICD-10-CM diagnosis codes D59.3, D59.5, G70.00, G36.0

## Billing

HCPCS code J1300 (injection, eculizumab, 10 mg)

## Prescribing Restrictions

Frequency of billing = 900 mg/90 units weekly for the first four weeks, followed by 1,200 mg/120 units for the fifth dose one week later, then 1200 mg /120 units every two weeks thereafter
Maximum billing unit(s) = 1,200 mg = 120 units

# Edaravone

Edaravone is a free-radical scavenger in solution for intravenous (IV) administration.

## Indications

Edaravone is reimbursable for the treatment of amyotrophic lateral sclerosis (ALS). The mechanism of therapeutic action is unknown; however, edaravone is a free-radical scavenger that may reduce oxidative stress of motor neurons, which has been implicated in the pathogenesis of ALS. In randomized controlled trials, edaravone has been found to slow functional deterioration in some ALS patients.

## Dosage

Edaravone is administered by IV infusion as follows:

- Initial treatment cycle: 60 mg IV given daily for 14 days of a 28-day treatment cycle on an intermittent schedule (14 days on and 14 days off).
- Subsequent treatment cycles: 60 mg IV given daily for 10 days out of a 14-day period of a 28 day-treatment cycle on an intermittent schedule (14 days on and 14 days off).

## Age

18 years and older

## Authorization

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

The TAR should include clinical documentation that demonstrates the following:

- The service is medically necessary.
- The patient has been diagnosed with definite or probable ALS based on the El Escorial/Airlie House revised criteria or Awaji criteria.
- The physician's legible, complete, and signed treatment plan/order for edaravone.

For continued authorization, the TAR should include clinical documentation that edaravone use has slowed the progression of ALS, and the patient's overall function has improved or is superior relative to that projected for the natural course of ALS.

### Required Codes

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

- G12.21 (Amyotrophic lateral sclerosis)

### Billing

HCPCS code J1301 (injection, edaravone, 1 mg)

One (1) unit of J1301 = 1 mg of edaravone injection solution

## 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.

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

- Must be used for all FDA approved indications and dosages
- Patient has a clinical diagnosis of Primary Hemophagocytic Lymphohistiocytosis (HLH) as confirmed by one of the following:
  - Genetic testing of gene mutation known to cause primary HLH (e.g., PRF1, UNC13D, STX11, or STXBP2); or
  - Meets at least 5 out of 8 of the following diagnostic criteria of primary HLH:
    - ❖ Fever
    - ❖ Splenomegaly
    - ❖ Cytopenias (especially anemia and thrombocytopenia)
    - ❖ Hypertriglyceridemia and/or hypofibrinogenemia››

- ❖ ‹‹Hemophagocytosis in bone marrow, spleen, or lymph nodes
- ❖ Low or absent natural killer (NK) cell activity
- ❖ Ferritin less than 500 mcg/L
- ❖ Soluble CD25 (i.e., soluble interleukin-2 receptor) ≥2,400 U/mL

- Must be prescribed by on in consultation with a hematologist or oncologist or a physician specialized in the treatment of HLH.
- Documentation of baseline evaluation of cardiac function (ie, electrocardiogram and echocardiogram)
- Patient has tried and failed, has inadequate response, or a contraindication to a conventional therapy such as dexamethasone and etoposide, with or without cyclosporine, or patient has a refractory, recurrent or progressive disease following conventional therapy.
- Emapalumab will be used in combination with dexamethasone if dexamethasone naïve; initiating the dexamethasone 1 day before emapalumab.
- Patient has not received hematopoietic stem cell transplantation (HSCT)
- Patient does not have any of the following:
  - Diagnosis of secondary Haemophagocytic Lymphohistiocytosis consequent to a proven rheumatic or neoplastic disease.
  - Active Mycobacteria, Histoplasma Capsulatum, Shigella, Salmonella, Campylobacter and Leishmania infections.
  - Concomitant disease or malformation severely affecting the cardiovascular, pulmonary, liver or renal functions

**Initial approval is for six months.**››

‹‹**Reauthorization:**

Continued therapy is approvable when the following criteria are met:

- Patient continues to meet initial coverage criteria
- Patient has shown clinical response as evidenced by HLH improvement, stabilization or lack of progression as evidenced by one of the following:
  - Clinical and laboratory criteria has shown no progression of HLH
  - Improvement (>50% change from baseline) of at least 3 HLH clinical and laboratory criteria (including CNS involvement).
  - Complete response defined as normalization of all HLH abnormalities
  - Partial response defined as normalization of ≥3 HLH abnormalities
- Patient does not have cardiac complications from inflammation or chemotherapy.

**Reauthorization is for 12 months**››

## Billing

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

## Suggested Codes

ICD-10 CM diagnosis code D76.1

## Prescribing Restrictions

Frequency of billing equal ‹‹1-10 mg/kg/dose›› 2 times per week

# Emicizumab-kxwh

Emicizumab-kxwh is a bispecific factor IXa-directed and factor X-directed antibody solution for subcutaneous (SQ) administration.

## Indications

Emicizumab-kxwh is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

## Age

All ages

## Dosage

The recommended dose is a 3 mg/kg SQ injection administered once weekly for four weeks, followed by a 1.5 mg/kg SQ injection administered once weekly thereafter.

## Authorization

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

- The TAR must include clinical documentation that demonstrates the following criteria:
- The service is medically necessary.
- The patient has a documented diagnosis of congenital factor VIII deficiency (hemophilia A).
- The patient has developed high-titer factor VIII inhibitors (≥5 Bethesda units [Bu]).
- The physician's legible, complete, and signed treatment plan/order for emicizumab-kxwh as a routine prophylaxis to prevent bleeding episodes associated with hemophilia A with factor inhibitors.

## Required Codes

One of the following ICD-10-CM diagnosis codes is required for reimbursement:

- D66 (Hereditary factor VIII deficiency)
- D68.311 (Acquired hemophilia)

## Billing

HCPCS code J7170 (injection, emicizumab-kxwh, 0.5 mg)
One (1) unit of J7170 = 0.5 mg of emicizumab-kxwh solution

# Enzyme Replacement Drugs

In the early 1960s, the first lysosomal storage disease was identified. Since then over 40 such diseases have been reported. The common feature is that enzyme deficiency leads to accumulation of undegraded macromolecules and lysosomal engorgement, resulting in organ dysfunction. Enzyme replacement drugs have been developed for many of these diseases. The following enzyme replacement drugs are benefits of the Medi-Cal program:

- Agalsidase Beta
- Alglucosidase Alfa
- Cerliponase Alfa
- Elosulfase Alfa
- Galsulfase
- Idursulfase
- Imiglucerase
- Laronidase
- Velaglucerase Alfa
- Vestronidase Alfa-vjbk

Authorization requirements for enzyme replacement drugs are described below. On the following pages the drugs are listed individually with information about their usage, dosage and billing requirements.

**Note:** Pharmacy providers of enzyme replacement therapy drugs may bill Medi-Cal directly using the National Drug Code (NDC) for the medication. This is a special Assignment of Benefit (AOB) exception to the DHCS policy restricting the reimbursement of all physician administered drugs to physicians and clinics. Pharmacy providers must submit a *Treatment Authorization Request* (TAR) to the TAR Processing Center, with the supporting documentation listed below. In addition, the pharmacy must include on the TAR the name of the physician to whom the medication will be released, or the name of the authorized representative specifically identified by the prescribing physician to receive the medication on his/her behalf. Pharmacies may not release the medication to anyone other than the prescribing physician without documented authorization from the prescribing physician identifying the specific agent authorized to receive the medication.

## Authorization

An approved TAR is required for reimbursement for each of these drugs. The TAR must be submitted to the TAR Processing Center.

For the initial TAR the following supporting documentation must be submitted:

- Subjective findings (complaints)
- Objective findings (exams, lab results)
  - Enzyme levels or other laboratory testing
  - DNA mutation analysis
  - Medical history
- Physical examination
- Complications (for example, bony changes or kidney failure)
- Quality of life issues (for example, severe, unremitting pain or extreme fatigue)
- Identified licensed practitioner who will administer infusion therapy, coordinate care, and their
  - Plan: Include the treatment plan including the genetic evaluation and counseling information for the patient and family members.
  - Goal: Include specific information about the desired outcome; for example, to slow the progression of the disease, to allow regular attendance at work or school or to significantly improve the quality of life.

Initial TAR approval may be for up to six months and renewal TARs may be approved for up to one year. Renewal TARs must include follow-up information such as any significant changes in physical findings, laboratory parameters, symptoms and/or quality of life.

## Agalsidase Beta

Fabry disease is an X-linked genetic disorder of glycosphingolipid metabolism. Deficiency of the lysosomal enzyme alpha-galactosidase-A leads to progressive accumulation of glycosphingolipids, predominantly GL-3, in many body tissues, starting early in life and continuing over decades. Agalsidase beta is a recombinant form of the enzyme alpha-galactosidase-A, which is required for the hydrolysis of GL-3 and other glycosphingolipids. In clinical trials of limited duration, agalsidase been noted to reduce tissue inclusions of GL-3. It is believed that long-term enzyme replacement may reduce clinical manifestations of renal failure, cardiomyopathy, and stroke.

Indications

For use in patients with Fabry disease.

Authorization

The TAR must include a diagnosis of Fabry disease. For other TAR requirements, see "Authorization" near the beginning of the "Enzyme Replacement Drugs" topic in this section.

Dosage

The recommended dose is 1 mg/kg every two weeks.

Billing

HCPCS code J0180 (injection, agalsidase beta, 1 mg).

## Alglucosidase Alfa

Pompe disease is an inherited disorder of glycogen metabolism caused by the absence or marked deficiency of the enzyme lysosomal acid maltase (alfa glucosidase). In the infantile-onset form, Pompe disease results in intralysosomal accumulation of glycogen in various tissues, particularly cardiac and skeletal muscles, and hepatic tissues, leading to the development of cardiomyopathy, progressive muscle weakness, and impairment of respiratory function. In the juvenile and adult-onset forms, intralysosomal accumulation of glycogen is limited primarily to skeletal muscle, resulting in progressive muscle weakness. Death in all forms is usually related to respiratory failure. Alglucosidase alfa provides an exogenous source of the enzyme lysosomal acid maltase.

Indications

Alglucosidase alfa (Lumizyme®) is used for treatment of all patients with Pompe disease.

- Myozyme® is used for treatment of patients younger than 8 years of age with infantile onset Pompe disease.

Authorization

The TAR must include a diagnosis of Pompe disease. For other TAR requirements, see "Authorizations" near the beginning of the "Enzyme Replacement Drugs" topic in this section.

Dosage

The recommended dose is 20 mg/kg every two weeks.

Billing

HCPCS code J0220 (injection, alglucosidase alfa, 10 mg, not otherwise specified). Use this code for Myozyme.

HCPCS code J0221 (injection, algucosidase alfa, [Lumizyme], 10 mg).

The correct National Drug Code (NDC) must be included on claims in order to correctly price the drug.

## Cerliponase Alfa

Cerliponase alfa is a hydrolytic lysosomal N-terminal tripeptidyl peptidase enzyme for central nervous system (CNS) intraventricular infusion.

Indication

Cerliponase alfa slows the loss of ambulation in symptomatic pediatric and adolescent patients with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

Neuronal ceroid lipofuscinosis (NCL) includes a group of lysosomal storage disorders that affect the nervous system. CLN2 is an inherited autosomal recessive disorder, caused by changes in the TPP1 gene.

Symptoms of CLN2 generally develop between 2 and 4 years of life, but can present at an older age. Symptoms are progressive and may include intractable seizures, ataxia, myoclonus, vision loss, and developmental delays in speech, cognition, motor function, etc.

Age

3 years and older

Dosage

300 mg administered once every other week by a CNS intraventricular infusion pump via a surgically implanted reservoir and catheter.

Authorization

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

The TAR must include clinical documentation that demonstrates the following:

1. The service is medically necessary to treat symptomatic late infantile CLN2, also known as TTP1 deficiency.
2. Additional criteria listed under “Authorization” near the beginning of the “Enzyme Replacement Drugs” topic in this section.
3. The physician’s legible, complete, and signed treatment plan/order for cerliponase alfa.

Required Codes

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

E75.4 (Neuronal ceroid lipofuscinosis)

Billing

HCPCS code J0567 (injection, cerliponase alfa, 1 mg)

One (1) unit of J0567 = 1 mg of cerliponase alfa enzyme

## Elosulfase Alfa

Mucopolysaccharidosis IV (A and B) is also known as Morquio syndrome. This disorder consists of two forms with similar clinical findings and autosomal inheritance. The clinical features result from accumulation of keratin sulfate (KS) and chondroitin 6 sulfate (C6S). Morquio syndrome is characterized by skeletal involvement, typically presenting as short stature at approximately one year of age. Respiratory problems often develop due to cord compression and the restrictive effects of skeletal disease. Both types of Morquio syndrome can have severe or mild forms. Mildly affected patients may survive into the seventh decade. Elosulfase alfa is intended to provide the exogenous enzyme N-acetylgalactosamine-6-sulfatase that will be taken up into the lysosomes and increase the catabolism of the glycosaminoglycans KS and C6S.

Indications

For use in patients with Mucopolysaccharidosis type IV A (Morquio A).

Authorization

The TAR must include a diagnosis of Mucopolysaccharidosis IV A. For additional details regarding authorization for this drug, see “Authorization” under the “Enzyme Replacement Drugs” topic in this manual section.

Dosage

The recommended dose is 2 mg/kg once a week.

Billing

HCPCS code J1322 (injection, elosulfase alfa, 1 mg).

## Eptinezumab-jjmr injection (Vyepti™)

Eptinezumab-jjmr is a humanized immunoglobulin G1 (IgG1) monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Vyepti 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 one of the following:
  - Episodic migraine defined as 4 to 14 headache days per month, at least four of which were migraine days during the previous three-month period; or
  - Chronic migraine defined as 15 to 26 headache days per month, at least eight of which were migraine days for over three months
- Patient must have tried and failed or is intolerant to or has contraindication to at least one drug from two oral classes used for migraine prophylaxis, including antiepileptic medications, beta-blockers, calcium channel blockers or antidepressants
- Must not be taken in combination with any other monoclonal antibody targeting the CGRP pathway, such as Ajovy (fremanezumab), Emgality (galcanezumab), Aimovig (erenumab), Nurtec ODT (rimegepant) and Ubrelvy (ubrogepant).

**Initial authorization is for six months**

Continued therapy:

- Patient continues to meet initial approval criteria
- Patient has experienced a positive clinical response to therapy as demonstrated by a reduction in headache frequency and/or severity

**Reauthorization is for twelve months**

Age Limits

Must be 18 years of age or older

Billing

HCPCS code J3032 (injection, eptinezumab-jjmr,1 mg)

Prescribing Restrictions

Frequency of billing = 300 mg/300 units every three months

Maximum billing unit(s) = 300 mg/300 units

**Note:** Vyepti is available through a limited distribution network of specialty distributors and specialty pharmacies.

**Vyepti is available through these authorized specialty distributors:**

ASD healthcare (hospitals)
Phone: 800-746-6273
Fax: 800-547-9413
www.asdhealthcare.com/home

Besse Medical
(physician offices and clinics)
Phone: 800-543-2111
Fax: 800-543-8695
https://www.besse.com/home

Oncology Supply
(physician offices and clinics)
Fax: 800-248-8205
www.oncologysupply.com/contact
Phone: 800-633-7555

McKesson Plasma & Biologics
(hospitals and alternate sites of care)
Phone: 877-625-2566
Fax: 888-752-7626
connect.mckesson.com

McKesson Specialty Care Division
(physician offices)
Phone: 855-477-9800
Fax: 800-800-5673
mscs.mckesson.com

**Vyepti is available through the following specialty pharmacies:**

Alliance Rx Walgreens Prime
Phone: 855-244-2555
Fax: 877-828-3939
alliancerxwp.com/referral-forms

Orsini Healthcare
Phone: 800-259-7145
Fax: 877-892-3019
orsinihealthcare.com/enrollment-forms

## Galsulfase

Mucopolysaccharidosis VI (Maroteaux-Lamy syndrome) is characterized by the absence or marked reduction in N–acetylgalactosamine-4-sulfatase. The sulfatase deficiency results in accumulation of partially degraded glycosaminoglycans, dermatan sulfate, and chondroitin 4-sulfate. This accumulation leads to widespread cellular, tissue, and organ dysfunction. Inheritance is autosomal recessive. Galsulfase is intended to provide an exogenous enzyme that will be taken up into lysosomes and increase the catabolism of glycosaminoglycans.

Indications

For use in patients with Mucopolysaccharidosis VI.

Authorization

The TAR must include a diagnosis of Mucopolysaccharidosis VI. For additional details regarding authorization for this drug, see “Authorization” under the “Enzyme Replacement Drugs” topic in this manual section.

Dosage

The recommended dose is 1 mg/kg once a week.

Billing

HCPCS code J1458 (injection, galsulfase, 1 mg).

## Givosiran (Givlaari)

Givosiran is a double-stranded small interfering RNA that causes degradation of aminolevulinate synthase 1 (ALAS1) mRNA in hepatocytes through RNA interference, reducing the elevated levels of liver ALAS1 mRNA. This leads to reduced circulating levels of neurotoxic intermediates aminolevulinic acid (ALA) and porphobilinogen (PBG), factors associated with attacks and other disease manifestations of acute hepatic porphyria (AHP).

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Givosiran is considered medically appropriate if all of the following criteria are met:

- Must be for FDA-approved indications and dosages
- Patient must be 18 years of age or older
- Patient must have a documented diagnosis of AHP, including acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria or ALA dehydratase deficient porphyria (ADP)
- Patient has a documentation of elevated urinary or plasma PBG and/or ALA within the past year
- The patient is not anticipating having a liver transplant
- The patient does not have a history of recurrent pancreatitis
- Documentation of a minimum of two porphyria attacks requiring hospitalization, urgent healthcare visit, or intravenous hemin administration in the previous six months

Initial authorization is for 12 months

**Reauthorization**

- Patient continues to meet initial approval criteria
- Patient shows absence of unacceptable toxicity from the drug (e.g. severe or clinically significant hepatic toxicity [transaminase elevations]), severe renal toxicity (increases in serum creatinine levels and decreases in estimated glomerular filtration rate [eGFR], etc.)
- Patient has shown a clinical response to therapy as evidenced by a reduction in the rate of porphyria attacks that required hospitalizations, urgent healthcare visits, or intravenous hemin administration

Reauthorization is for 12 months

Age Limits

Must be 18 years of age or older

Billing

HCPCS code J0223 (injection, givosiran, 0.5 mg)

Suggested ICD-10 Diagnosis Codes

E80.20, E80.21, E80.29

Prescribing Restrictions

Frequency of billing = 2.5 mg/kg every month

## Idursulfase

Hunter syndrome (Mucopolysaccharidosis II, MPS II) is an X-linked recessive disease caused by insufficient levels of the lysosomal enzyme iduronate-2-sulfatase. This enzyme cleaves the terminal 2-0-sulfate moieties from dermatan sulfate and heparan sulfate. Due to the missing or defective iduronate-2-sulfatase enzyme in patients with Hunter syndrome, dermatan sulfate and heparan sulfate progressively accumulate in the lysosomes of a variety of cells, leading to cellular engorgement, organomegaly, tissue destruction, and organ system dysfunction.

Indications

For use in patients with Hunter syndrome.

Authorization

The TAR must include a diagnosis of Hunter syndrome. For additional details regarding authorization for this drug, see “Authorization” under the “Enzyme Replacement Drugs” topic in this manual section.

Dosage

The recommended dose is 0.5 mg/kg once a week.

Billing

HCPCS code J1743 (injection, idursulfase, 1 mg).

## Imiglucerase

Gaucher disease is classically categorized into three main types (I, II and III) and is characterized by a deficiency of beta-glucocerebrosidase activity, resulting in accumulation of glucocerebroside in tissue macrophages which become engorged and are typically found in the liver, spleen, and bone marrow and occasionally in lung, kidney, and intestine. Secondary hematologic sequelae include severe anemia and thrombocytopenia in addition to the characteristic progressive hepatosplenomegaly, skeletal complications, including osteonecrosis and osteopenia with secondary pathological fractures. Imiglucerase catalyzes the hydrolysis of glucocerebroside to glucose and ceramide. In clinical trials, imiglucerase improved anemia and thrombocytopenia, reduced spleen and liver size, and decreased cachexia.

Indications

For long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of Type 1 Gaucher disease that results in one or more of the following conditions:

- Anemia
- Thrombocytopenia
- Bone disease
- Hepatomegaly or splenomegaly

Authorization

The TAR must include a diagnosis of Type 1 Gaucher disease. For additional details regarding authorization for this drug, see “Authorization” under the “Enzyme Replacement Drugs” topic in this manual section.

Dosage

Recommended dosages range from 2.5 units/kg three times a week to 60 units/kg every two weeks. The dose should be individualized to each patient with a maximum allowable dose of 818 billed units per day. If necessary, a TAR may override this maximum dose with justification that the patient weighs 300 lbs or more.

Billing

HCPCS code J1786 (injection, imiglucerase, per10 units).

## Laronidase

Mucopolysaccharidosis I (MPS I) is characterized by the deficiency of alpha-L-iduronidase, a lysosomal hydrolase which catalyzes the hydrolysis of terminal alpha-L-iduronic acid residues of dermatan sulfate and heparan sulfate. Reduced or absent alpha-L-iduronidase activity results in the accumulation of dermatan sulfate and heparan sulfate throughout the body and leads to widespread cellular, tissue, and organ dysfunction. MPS I includes Hurler, Hurler-Scheie, and Scheie syndromes that represent the spectrum of severity. The clinical phenotype covers a broad spectrum and patients with severe, intermediate, and mild features are classified as Hurler, Hurler-Scheie, and Scheie syndromes, respectively.

Indications

Laronidase is indicated for patients with Hurler and Hurler-Scheie forms of MPS I and for patients with the Scheie form who have moderate to severe symptoms. The risks and benefits of treating mildly affected patients with the Scheie form have not been established.

Authorization

The TAR must include a diagnosis of either Hurler and Hurler-Scheie forms of MPS I, or the Scheie form with moderate to severe symptoms. For additional details regarding authorization for this drug, see “Authorization” under the “Enzyme Replacement Drugs” topic in this manual section.

Dosage

The recommended dose is 0.58 mg/kg once a week.

Billing

HCPCS code J1931 (injection, laronidase, 0.1 mg).

## Velaglucerase Alfa

Gaucher disease is classically categorized into three main types (I, II and III) and is characterized by a deficiency of beta-glucocerebrosidase activity, resulting in accumulation of glucocerebroside in tissue macrophages that become engorged and are typically found in the liver, spleen and bone marrow and occasionally in lung, kidney and intestine. Secondary hematologic sequelae include severe anemia and thrombocytopenia in addition to the characteristic progressive hepatosplenomegaly, skeletal complications, including osteonecrosis and osteopenia with secondary pathological fractures. Velaglucerase alfa catalyzes the hydrolysis of glucocerebroside to glucose and ceramide.

Indications

For use in patients 4 years of age or older with Type I Gaucher disease.

Authorization

The TAR must include a diagnosis of Type I Gaucher disease. For additional details regarding authorization for this drug, see “Authorization” under the “Enzyme Replacement Drugs” topic in this manual section.

Dosage

The recommended dose is 60 units/kg every other week as a 60-minute infusion.

Billing

HCPCS code J3385 (injection, velaglucerase alfa, 100 units).

Claims must include an invoice showing the cost of the drug.

## Vestronidase alfa-vjbk

Vestronidase alfa-vjbk is a recombinant human lysosomal beta glucuronidase enzyme for intraventricular infusion.

Indications

Vestronidase alfa-vjbk is used to treat patients with Mucopolysaccharidosis VII (MPS VII or "Sly Syndrome").

Mucopolysaccharidoses includes a group of inherited lysosomal storage disorders in which the body cannot properly break down mucopolysaccharides, specifically glycosaminoglycans (GAGs), long chains of sugar molecules that exist naturally in the body. MPS VII is an autosomal recessive disorder, caused by mutations in the glucuronidase beta (GUSB) gene. This gene defect causes a deficiency of β-glucuronidase, an enzyme required for the body's normal metabolism of GAGs. Without β-glucuronidase, GAGs abnormally accumulate within the lysosomes of body cells and eventually cause tissue and organ dysfunction.

Symptoms of MPS VII are progressive and variable. Prominent features include macrocephaly, hydrocephalus, musculoskeletal abnormalities, vision and hearing loss, hepatosplenomegaly, heart and lung disease, and developmental and cognitive delays.

The effect of vestronidase alfa-vjbk on the central nervous system (CNS) manifestations of MPS VII has not been determined.

Age

All ages

Dosage

The recommended dose is 4 mg/kg administered IV every 2 weeks.

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 MPS VII.
- Additional criteria listed under "Authorization" near the beginning of the "Enzyme Replacement Drugs" topic in this section.
- The physician's legible, complete, and signed treatment plan/order for vestronidase alfa-vjbk.

Required Codes

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

- E76.29 (other mucopolysaccharidoses [including MPS VII])

Billing

HCPCS code J3397 (injection, vestronidase alfa-vjbk, 1 mg)

One (1) unit of J3397 = 1 mg of vestronidase alfa-vjbk enzyme

# Epoetin Alfa

Epoetin alfa (EA) is a 165-amino acid erythropoiesis-stimulating glycoprotein manufactured by recombinant DNA technology. The product contains the identical amino acid sequence of isolated natural erythropoietin and stimulates erythropoiesis by the same mechanism as endogenous erythropoietin.

## Indications

For the treatment of anemia due to:

- Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis.
- Anti-retroviral therapy in HIV-infected patients.
- The effects of myelosuppressive chemotherapy in patients with non-myeloid malignancies and upon initiation, there is a minimum of two additional months of planned chemotherapy.
- Reduction of allogeneic RBC transfusion in patients undergoing elective, noncardiac, nonvascular surgery.
- Myelodysplastic syndromes.

## Limitations of Usage

EA has not been shown to improve quality of life, fatigue, or patient well-being.

EA is not indicated for use:

- In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
- In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- In patients scheduled for surgery who are willing and able to donate autologous blood.
- In patients undergoing cardiac or vascular surgery.
- As a substitute for RBC transfusions in patients who require immediate correction of anemia.

In the appropriate circumstances, EA may be self-administered.

## CKD Patients on Dialysis

EA treatment may be initiated when the hemoglobin level is less than 10 g/dL, taking into consideration specific patient characteristics such as functional and cognitive status, life-expectancy, and other factors. If the hemoglobin level approaches or exceeds 11 g/dL, it is recommended that the dose of epoetin alfa be reduced or interrupted.

## CKD Patients Not on Dialysis

EA treatment may be initiated when the hemoglobin level is less than 10 g/dL and the following conditions apply:

- The rate of hemoglobin decline indicates the likelihood of requiring a RBC transfusion and,
- Reducing the risk of alloimmunization and/or other RBC transfusion-related risks is a goal

If the hemoglobin level exceeds 10 g/dL, it is recommended that the dose of epoetin alfa be reduced or interrupted.

## Non-CKD Conditions

Certain non-CKD conditions may qualify patients to receive epoetin alfa therapy:

- Anti-retroviral therapy treated HIV-infected patients may receive epoetin alfa should they develop symptomatic anemia and have serum erythropoietin concentrations that are less than 500 IU/L. EA should be withheld if the hemoglobin level exceeds 12 g/dL and therapy resumed at a dose 25% below the previous dose when the hemoglobin declines to less than 11 g/dL.
- For patients with chemotherapy-associated anemia in non-myeloid malignancies, EA is recommended as a treatment option when the hemoglobin level has decreased below 10 g/dL and if there is a minimum of two additional months of planned chemotherapy.
- Patients undergoing elective noncardiac, nonvascular surgery to reduce allogeneic RBC transfusions may receive epoetin alfa if they are unwilling or unable to donate autologous blood. Patients should have perioperative hemoglobin between 10 and 13 g/dL.
- Patients with a myelodysplastic syndrome should have an erythropoietin level equal to or less than 500 IU/L and low or intermediate-1 risk International Prognostic Scoring System score (1.0 or less).

## Required ICD-10-CM Codes

ICD-10-CM diagnosis codes are required on the claim form in the *Diagnosis or Nature of Illness or Injury* field (Box 21) of the *CMS-1500* form or in the *Diagnosis Codes* field (Box 66–67) of the *UB-04* form.

- CKD patients with anemia on dialysis require N18.6 for HCPCS code Q4081
- CKD patients with anemia not on dialysis require N18.1 thru N18.5 or N18.9 for HCPCS code J0885
- Anti-retroviral therapy treated HIV-infected patients with symptomatic anemia requires B20 or B97.35 for HCPCS code J0885
- Chemotherapy-associated anemia in non-myeloid malignancies requires D64.81 for HCPCS code J0885
- Patients undergoing elective noncardiac, nonvascular surgery requires Z41.8 for HCPCS code J0885
- Patients with a myelodysplastic syndrome require D46.0 thru D46.9 for HCPCS code J0885

## Dosage

Evaluate the iron status in all patients before and during treatment and maintain iron repletion. Correct or exclude other causes of anemia (for example, vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) before initiating epoetin alfa.

The dose of EA varies according to the condition being treated. Please refer to appropriate medical literature for specific dosage recommendations.

## Billing

The following HCPCS codes should be used when billing epoetin alfa:

| HCPCS Code | Description |
|---|---|
| J0885 | Injection, epoetin alfa, for non-ESRD use, 1,000 units |
| Q4081 | Injection, epoetin alfa, for ESRD on dialysis, 100 units |

If EA is administered by the provider, the claim must include current and previous:

- EA dose
- Patient weight in kilograms
- Hemoglobin levels

If EA is self-administered by the patient, the claim must include:

- A statement that the drug was provided to the patient for self-administration
- The date and quantity of drug given to the patient
- EA doses, hemoglobin levels and patient weight in kilograms for the previous three months

Documentation may be included in the *Remarks* field (Box 80) on the *UB-04* or the *Additional Claim Information* field (Box 19) on the *CMS-1500*, or on an attachment to the claim.

If EA is administered outside of the general guidelines above or dosage is more than 90,000 units per week, documentation must be submitted in order to establish medical necessity.

# Epoetin alfa-epbx

Epoetin alfa-epbx is a erythropoiesis-stimulating glycoprotein solution for intravenous (IV) or subcutaneous (SQ) injection. Epoetin alfa-epbx is biosimilar to epoetin alfa.

## Indications

Epoetin alfa-epbx is indicated for treatment of anemia due to the following:

- Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis.
- The effect of zidovudine administered at ≤4,200 mg/week in patients with HIV infection with endogenous serum erythropoietin levels of ≤500 mUnits/mL.
- The effect of concomitant myelosuppressive chemotherapy in patients with non-myeloid malignancies and upon initiation, there is a minimum of two additional months of planned chemotherapy.

Epoetin alfa-epbx is indicated to reduce the need for allogeneic red blood cell (RBC) transfusions in patients with perioperative hemoglobin levels between 10 and 13 g/dL who are at high risk for perioperative blood loss from elective, non-cardiac, nonvascular surgery.

Epoetin alfa-epbx is not indicated for use:

- In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
- In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- In patients with cancer receiving myelosuppressive chemotherapy in whom the anemia can be managed by transfusion.
- In patients scheduled for surgery who are willing to donate autologous blood.
- In patients undergoing cardiac or vascular surgery.
- As a substitute for RBC transfusions in patients who require immediate correction of anemia.

## Age

All ages

## Dosage

The recommended dose of epoetin alfa-epbx depends on the treatment indication and the patient's age, weight, pre- and post-treatment hemoglobin levels, and response to therapy.

## Authorization

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

## Required Codes

For HCPCS code Q5105, ICD-10-CM diagnosis code D63.1 (Anemia in chronic kidney disease) is required for reimbursement.

For HCPCS code Q5106, one of the following ICD-10-CM diagnosis codes is required for reimbursement:

- B20 (Human immunodeficiency virus [HIV] disease)
- B97.35 (Human immunodeficiency virus type 2 [HIV 2] as the cause of diseases classified elsewhere)
- D46.0 thru D46.9 (Myelodysplastic syndromes)
- D61.1 (Drug-induced aplastic anemia)
- D61.810 (Antineoplastic chemotherapy induced pancytopenia)
- D61.811 (Other drug-induced pancytopenia)
- D63.0 (Anemia in neoplastic disease)
- D63.8 (Anemia in other chronic diseases classified elsewhere)
- D64.81 (Anemia due to antineoplastic chemotherapy)
- Y83.0 thru Y83.9 (Surgical operation and other surgical procedures as the cause of abnormal reaction of the patient or of later complication, without mention of misadventure at the time of the procedure)

## Billing

HCPCS code Q5105 (injection, epoetin alfa, biosimilar [Retacrit] [for ESRD on dialysis], 100 units)
One (1) unit of Q5105 = 100 units of epoetin alfa-epbx

HCPCS code Q5106 (injection, epoetin alfa, biosimilar [Retacrit] [for non-ESRD use], 1000 units)
One (1) unit of Q5106 = 1000 units of epoetin alfa-epbx

# Eravacycline (Xerava)

Eravacycline is a fluorocycline antibacterial within the tetracycline class of antibacterial drugs. Eravacycline disrupts bacterial protein synthesis by binding to the 30S ribosomal subunit thus preventing the incorporation of amino acid residues into elongating peptide chains.

## Indications

All FDA-approved indications

## Dosage

FDA-approved dosages

## TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement. The TAR must meet the following criteria for approval:

- FDA approved indications and dosages
- Must be 18 years of age or older
- Must show documentation for a diagnosis of complicated intra-abdominal infections (cIAIs) caused by one of the following susceptible microorganisms: Escherichia coli, Klebsiella pneumoniae, Citrobacter freundii, Enterobacter cloacae, Klebsiella oxytoca, Enterococcus faecalis, Enterococcus faecium, Staphylococcus aureus, Streptococcus anginosus group, Clostridium perfringens, Bacteroides species and Parabacteroides distasonis, and
- Must show documentation of culture and sensitivity tests showing that the infection is not susceptible to the formulary alternatives, or documentation of previous intolerance or contraindication to all formulary alternatives with shown susceptibility on the culture and sensitivity tests, or
- Documentation showing that treatment was initiated during a recent hospitalization or other acute care treatment
- May be authorized for a maximum of 14 days

## Age Limits

Must be 18 years of age or older

## Billing

HCPCS code J0122 (injection, eravacycline, 1 mg)

## Prescribing Restrictions

Frequency of billing = Every 14 days
Maximum billing units = 6,364 mg = 6,364 units

# Ertapenem

Ertapenem inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins; which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Bacteria eventually lyse due to ongoing activity of cell wall autolytic enzymes (autolysins and murein hydrolases) while cell wall assembly is arrested.

## Indications

All FDA-approved indications.

## Dosage

FDA approved dosages.

## TAR Requirement

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

## TAR Criteria

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

- Must be used for FDA-approved indications and dosages
- Patient must be diagnosed with one of the following moderate to severe infections caused by susceptible bacteria:
  - Complicated intra-abdominal infections.
  - Complicated skin and skin structure infections, including diabetic foot infections without osteomyelitis.
  - Community-acquired pneumonia.

  - Complicated urinary tract infections including pyelonephritis.
  - Acute pelvic infections including postpartum endomyometritis, septic abortion and post-surgical gynecologic infections
- Must show documentation for justification of failure to use formulary alternatives such as Beta-lactams (e.g., ceftriaxone, Augmentin), fluoroquinolones (e.g., ciprofloxacin), vancomycin, etc., or previous intolerance, allergy or contraindication to all formulary alternatives or that selection is based on local epidemiology and susceptibility patterns; or
- Ertapenem is being used for the prophylaxis of surgical site infection following elective colorectal surgery.

### Billing

HCPCS code J1335 (Injection, ertapenem sodium, 500 mg).

### Prescribing Restrictions

Frequency of billing = 1 gram/2 units daily for up to 14 days

Maximum billing unit(s) = 1 gram/2 units

## Etelcalcetide

Etelcalcetide (Parsabiv™) is a synthetic peptide that functions as an allosteric activator of the calcium-sensing receptor (CaSR) in the parathyroid gland.

Etelcalcetide specifically binds to and activates the CaSR, which reduces parathyroid hormone (PTH) secretion from the chief cells of the parathyroid gland, which enhances activation of the receptor by extracellular calcium. Activation of the CaSR on parathyroid chief cells decreases PTH secretion. The reduction in PTH is associated with a concomitant decrease in serum calcium and phosphate levels.

### Indications

Etelcalcetide indicated for the treatment of secondary hyperparathyroidism (HPT) in patients 18 years of age or older with chronic kidney disease (CKD) on hemodialysis.

### Authorization

A TAR is required for reimbursement.  Documentation of secondary HPT in patients with CKD on hemodialysis.

### Required Codes

ICD-10-CM diagnosis code N25.81 is required for every claim, as well as any of the following ICD-10-CM diagnosis codes: N18.11 thru N18.6, N18.9 and D63.1.

### Dosage

The recommended starting dose is 5 mg administered by IV bolus injection three times per week at the end of the hemodialysis treatment. Dose may be increased in 2.5 mg or 5 mg increments no more frequently than every four weeks. Etelcalcetide maintenance dosage should be individualized and determined by titration based on PTH and corrected serum calcium response, with a dose range between 2.5 thru 15 mg.

### Billing

HCPCS code J0606 (injection, etelcalcetide, 0.1 mg)

## Eteplirsen

Eteplirsen is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. Eteplirsen is designed to bind to exon 51 of dystrophin pre-mRNA, resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 51 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein.

### Indications

Eteplirsen is indicated for the treatment of DMD in patients 2 years of age or older who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Exondys 51™.

### Dosage

The recommended dosage is 30 milligrams per kilogram of body weight once weekly. Administer as an intravenous infusion over 35 to 60 minutes. Dilution required prior to administration.

Dosage forms and strengths:

- 100 mg/2 ml (50 mg/ml) in single-dose vial
- 500 mg/10 ml (50 mg/ml) in single-dose vial

### Required Codes

ICD-10-CM diagnosis code G71.0

### Billing

HCPCS code J1428 (injection, eteplirsen, 10 mg).

# Etonogestrel Implant

Refer to the *Family Planning* section in the appropriate Part 2 manual for billing instructions for etonogestrel contraceptive implant systems (HCPCS code J7307).

# Evinacumab-dgnb (Evkeeza™)

Evinacumab-dgnb is a recombinant human monoclonal antibody that binds to and inhibits ANGPTL3. ANGPTL3 is a member of the angiopoietin-like protein family that is expressed primarily in the liver and plays a role in the regulation of lipid metabolism by inhibiting lipoprotein lipase (LPL) and endothelial lipase (EL). Evinacumab-dgnb inhibition of ANGPTL3 leads to reduction in low density lipoprotein-cholesterol ( LDL-C), high density lipoprotein-cholesterol (HDL-C), and triglycerides (TG). Evinacumab-dgnb reduces LDL-C independent of the presence of LDL receptor (LDLR) by promoting very low-density lipoprotein (VLDL) processing and clearance upstream of LDL formation. Evinacumab-dgnb blockade of ANGPTL3 lowers TG and HDL-C by rescuing LPL and EL activities, respectively.

## Indications

All FDA-approved indications

## Dosage

FDA-approved dosages

## TAR Requirement

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

## TAR Criteria

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

- Must be used for FDA-approved indications and dosages
- Patient must be 12 years of age or older
- Patient has a diagnosis of homozygous familial hypercholesterolemia (HoFH) confirmed by at least one of the following:
  - Genetic testing showing mutations of pathogenic variants of the low-density lipoprotein receptor (LDL-R) gene, or pathogenic variants of the apolipoprotein (ApoB) gene, or homozygous mutations in the LDL-R adaptor protein-1

  - Patient has very high LDL-C (greater than 500 mg/dL untreated or greater than 300 mg/dL if on maximal lipid-lowering therapy), and cholesterol deposits in the first decade of life in the setting of a strong family history; AND physical manifestations such as xanthomas, xanthelasmas (cholesterol deposits in the eyelids or skin), or corneal arcus
  - Patient has a low-density lipoprotein-cholesterol (LDL-C) level of equal to or greater than 190 mg/dL, or lower with strong family histories and/or physical findings such as xanthomas, xanthelasmas (cholesterol deposits in the eyelids or skin), or corneal arcus
- If undergoing LDL apheresis, must have initiated LDL apheresis at least 3 months prior to treatment initiation and must have been on a stable weekly or every other week schedule and/or stable settings for at least 8 weeks
- Must be prescribed by or in consultation with a lipid specialist or other specialist experienced in the treatment of HoFH
- Patient must have tried and failed, is intolerant to or has a clinical contraindication to high dose statin therapy (with atorvastatin 80 mg or rosuvastatin 40 mg) or lower if indicated, and 10 mg ezetimibe
- Patient did not achieve their LDL-C goal after 3 months on statin and ezetimibe and Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor (for example: evolocumab) unless intolerant or clinically contraindicated
- Patient will take Evkeeza in combination with other LDL-C lowering therapies such as statins, ezetimibe, etc.
- Patient is not a pregnant or breastfeeding female

Initial authorization is for 6 months.

<u>Continued Therapy</u>

- Patient continues to meet initial coverage criteria
- Positive clinical response as evidenced by reduction of LDL-C from baseline,
- Patient continues treatment with other traditional low-density lipoprotein-cholesterol (LDL-C) lowering therapies (for example: statin, ezetimibe) in combination with Evkeeza.

Reauthorization is for 12 months

### Age Limit

Must be 12 years of age or older

### Billing

‹‹HCPCS code J1305 (injection, evinacumab-dgnb, 5 mg)››

### Required ICD-10-CM Diagnosis Codes

E78.01

### Prescribing Restriction(s)

Frequency of billing equals 15 mg/kg once monthly (every 4 weeks)

## Ferric Carboxymaltose

Ferric carboxymaltose is a colloidal iron hydroxide in complex with carboxymaltose, a carbohydrate polymer that releases iron.

### Indications

For the treatment of iron deficiency anemia in patients 18 years of age and older who have any of the following:

- Intolerance to oral iron
- Had unsatisfactory response to oral iron
- Non-dialysis dependent chronic kidney disease

### Dosage

The recommended dosage:

- For patients weighing 50 kg or more: 750 mg in two doses separated by at least seven days for a maximum cumulative dose not to exceed 1,500 mg per course
- For patients weighing less than 50 kg: two doses separated by at least seven days with each dose administered as 15 mg/kg body weight

### Billing

HCPCS code J1439 (injection, ferric carboxymaltose, 1 mg).

# ‹‹Ferric Derisomaltose (Monoferric®)

Ferric derisomaltose is a complex of iron (III) hydroxide and derisomaltose, an iron carbohydrate oligosaccharide that releases iron. Iron binds to transferrin for transport to erythroid precursor cells to be incorporated into hemoglobin.

## Indications

All FDA-approved indications

## Dosages

FDA-approved dosages

## TAR Requirement

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

## TAR Criteria

The TAR must include clinical documentation that demonstrates the following:

- Must be used for FDA-approved indications and dosages
- Patient must be 18 years of age or older
- Patient has a documented trial and failure or an intolerance or contraindication to formulary iron preparation injection alternatives such as Feraheme, Venofer, Injectafer as clinically appropriate; and
- Patient has a diagnosis of iron deficiency anemia and non-hemodialysis dependent chronic kidney disease (NDD-CKD); or
- Patient has a diagnosis of iron deficiency anemia and any of the following applies:
  - Patient has tried oral iron and it was ineffective or had unsatisfactory response or intolerable gastrointestinal side effects
  - Patient has a physiologic or anatomic abnormality that interferes with oral absorption or iron homeostasis (for example, inflammatory bowel disease, Crohn's disease, or gastric surgery); or
- Patient is a pregnant female; or
- Patient has a severe or ongoing blood loss; or
- Provider has other justifiable reason why Monoferric is clinically appropriate for the patient.

**Initial approval is for six months.**››

‹‹Reauthorization

- Patient continues to meet the initial coverage criteria
- Must submit recent laboratory results since the last administration of intravenous iron preparation to demonstrate a need for additional therapy

**Reauthorization will be for six months.**

## Age Limits

Must be 18 years of age or older

## Billing

HCPCS code J1437 (injection, ferric derisomaltose, 10 mg)

## Suggested ICD-10-CM Diagnosis Codes

Primary Diagnosis Codes:

D50.0, D50.1, D50.8, D50.9, D63.0, D63.1, D63.8, D64.81

Secondary Diagnosis Codes:

K50.0 thru K50.919, K51.0 thru K51.919, K90.0, K90.4, K90.9, N18.1 thru N18.4

## Prescribing Restrictions

Frequency of billing = 1,000 mg/100 units for one dose. May repeat dose if iron deficiency anemia reoccurs.

Maximum billing unit(s) = 1,000 mg/100 units››

# Ferumoxytol (Feraheme®)

Ferumoxytol consists of a superparamagnetic iron oxide that is coated with a carbohydrate shell, which helps to isolate the bioactive iron from plasma components until the iron-carbohydrate complex enters the reticuloendothelial system macrophages of the liver, spleen and bone marrow. The iron is released from the iron-carbohydrate complex within vesicles in the macrophages. Iron then either enters the intracellular storage iron pool (for example, ferritin) or is transferred to plasma transferrin for transport to erythroid precursor cells for incorporation into hemoglobin.

## Indications

All FDA-approved indications

### Dosages

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 Q0138 (injection, ferumoxytol, for treatment of iron deficiency anemia, 1 mg [non-ESRD use])

HCPCS code Q0139 (injection, ferumoxytol, for treatment of iron deficiency anemia, 1 mg [for ESRD on dialysis])

### Suggested ICD-10 Diagnosis Codes

D50.0, D50.1, D50.8, D50.9, D63.0, D63.1, D63.8, D64.81, N18.1 thru N18.6, N18.9.

### Prescribing Restrictions

Frequency of billing = Initial 510 mg/510 units dose followed by a second 510 mg/510 units dose three to eight days later.

Maximum billing unit(s) = 510 mg/510 units

## Fibrinogen (Human)

Fibrinogen (human) is a human fibrinogen concentrate for intravenous (IV) infusion.

### Indications

Fibrinogen (human) is used to treat acute bleeding episodes in patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

Fibrinogen (human) is not indicated for dysfibrinogenemia.

### Age

12 years and older

## Dosage

The recommended target fibrinogen plasma level is 100 mg/dL for minor bleeding and 150 mg/dL for major bleeding.

- When the fibrinogen level is known, the recommended dose is calculated as follows:
  - Dose (mg/kg body weight) = [Target fibrinogen level (mg/dL) – (minus) measured fibrinogen level (mg/dL)] ÷ 1.8 (mg/dL per mg/kg body weight)
- When the fibrinogen level is unknown, the recommended dose is of 70 mg/kg of body weight.
- If the plasma fibrinogen level is below the accepted lower limit of the target level (80 mg/dL for minor bleeding, 130 mg/dL for major bleeding), the dose is repeated until hemostasis is achieved.

## 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 an acute bleeding episode in a patient with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.
- The plasma fibrinogen levels and bleeding assessments taken and monitored during fibrinogen treatment.
- The physician's legible, complete, and signed treatment plan/order for fibrinogen (human) concentrate (Fibryga®).

## Required Codes

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

- D68.2 (Hereditary deficiency of other clotting factors [including congenital afibrinogenemia and hypofibrinogenemia])

## Billing

HCPCS code J7177 (injection, human fibrinogen concentrate [fibryga], 1 mg)

One (1) unit of J7177 equals 1 mg of human fibrinogen concentrate (Fibryga)

# Filgrastim

Filgrastim is a Medi-Cal benefit when used for patients with severe neutropenia.

## Dosage

The specific dosage of filgrastim is variable depending on which condition or disease is being treated.

## Required Codes

Filgrastim is reimbursable only with one of the following ICD-10-CM diagnosis codes:

| | | |
|---|---|---|
| C92.00 | C92.90 | D70.4 thru D70.9 |
| C92.30 | C92.A0 | D72.819 |
| C92.40 | C92.Z0 | Z48.290 |
| C92.50 | D46.0 thru D46.9 | Z51.11 |
| C92.60 | D70.0 thru D70.1 | Z94.81 |

## Billing

HCPCS code J1442 (injection, filgrastim [g-csf], excludes biosimilars, 1 microgram).

When billing for more than 1,200 mcg, providers must document in the *Remarks* field (Box 80)/*Additional Claim Information* field (Box 19) on the claim or on an attachment that the patient weighs more than 100 kg.

# Filgrastim-aafi (Nivestym™)

Colony-stimulating factors are glycoproteins which act on hematopoietic cells by binding to specific cell surface receptors and stimulating proliferation, differentiation commitment, and some end-cell functional activation.

Endogenous G-CSF is a lineage-specific colony-stimulating factor that is produced by monocytes, fibroblasts, and endothelial cells. G-CSF regulates the production of neutrophils within the bone marrow and affects neutrophil progenitor proliferation, differentiation, and selected end-cell functions (including enhanced phagocytic ability, priming of the cellular metabolism associated with respiratory burst, antibody-dependent killing, and the increased expression of some cell surface antigens). G-CSF is not species-specific and has been shown to have minimal direct in vivo or in vitro effects on the production or activity of hematopoietic cell types other than the neutrophil lineage.

## Indications

All FDA-approved indications

### Dosage

FDA-approved dosages

### Authorization

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

### Suggested ICD-10 Diagnosis Codes

D70.0, D70.1, D70.4, D70.8, D70.9 or Z51.11

### Billing

HCPCS code Q5110 (injection, filgrastim-aafi, biosimilar [Nivestym], 1 mcg)

## Filgrastim-sndz

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

### Indications

Filgrastim-sndz 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-sndz 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 Q5101 (injection, filgrastim-sndz, biosimilar, [Zarxio], 1 microgram).

One (1) unit of Q5101 equals 1 microgram of filgrastim-sndz

## Fomepizole

Fomepizole, 15 mg, is billed with HCPCS injection code J1451. Reimbursement is allowed up to a maximum of 140 units.

## Fosaprepitant

Fosaprepitant injection, 1 mg (HCPCS code J1453) has a maximum daily dosage of 150 mg. It is reimbursable when administered in combination with other antiemetic agents and is indicated for the following:

- Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy, including high-dose cisplatin
- Prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy

## Fremanezumab-vfrm (Ajovy)

Fremanezumab is a humanized monoclonal antibody that binds to calcitonin gene-related peptide (CGRP) ligand and blocks its binding to the receptor.

### Indications

All FDA-approved indications

### Dosage

FDA-approved dosages

### TAR Requirement

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

- Patient ≥ 18 years of old and not pregnant
- Patient has had a trial of at least one drug from two oral classes used for migraine prophylaxis, including antipileptic medications, beta-blockers or antidepressants
- Patient has a diagnosis of chronic migraine

### Age Limits

Must be 18 years of age or older

### Billing

HCPCS code J3031 (injection, fremanezumab-vfrm, 1 mg)

### Prescribing Restrictions

Frequency of billing equals Every month

Maximum billing units equals 225 mg equals 225 units

## Galsulfase

For detailed billing policy information about galsulfase, refer to the “Enzyme Replacement Drugs” topic in this manual section.

## GenVisc 850®

GenVisc 850 is a sterile, viscoelastic non-pyrogenic solution of purified, high molecular weight sodium hyaluronate (average of 850,000 daltons and a range of 620,000 to 1,170,000 daltons) having a pH of 6.8 to 7.8. Each 2.5 ml of GenVisc 850 contains 10 mg/ml of sodium hyaluronate dissolved in a physiological saline (1.0 percent solution). The sodium hyaluronate is derived from bacterial fermentation. Sodium hyaluronate is a poly-saccharide containing repeating disaccharide units of glucuronic acid and N-acetylglucosamine.

## Indication

GenVisc 850 is indicated for the treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative, non-pharmacologic therapy and simple analgesics, such as acetaminophen.

## Dosage

GenVisc 850 is administered by intra-articular injection. A treatment cycle consists of five injections given at weekly intervals. Strict aseptic administration technique must be followed. Inject the full 2.5 ml in one knee only. If treatment is bilateral, a separate syringe should be used for each knee.

## Required Codes

ICD-10-CM diagnosis codes:

| | | |
|---|---|---|
| M17.0 | M17.2 | M17.4 |
| M17.10 | M17.30 | M17.5 |
| M17.11 | M17.31 | M17.9 |
| M17.12 | M17.32 | |

## Billing

HCPCS code J7320 (hyaluronan or derivative, genvisc 850, for intra-articular injection 1 mg)

# Glucarpidase

Glucarpidase is a carboxypeptidase produced by recombinant DNA technology in genetically modified *Escherichia coli*. It hydrolyzes the carboxyl-terminal glutamate residue from folic acid and classical antifolates such as methotrexate and converts it to its inactive metabolites 4-deoxy-4-amino-N10-methylpteroic acid (DAMPA) and glutamate. Glucarpidase provides an alternate non-renal pathway for methotrexate elimination in patients with renal dysfunction during high-dose methotrexate treatment.

## Indications

Glucarpidase is indicated for the treatment of toxic plasma methotrexate concentrations (less than 1 micromole per liter) in patients with delayed methotrexate clearance due to impaired renal function.

### Limitation of Use

Glucarpidase is not indicated for use in patients who exhibit the expected clearance of methotrexate (plasma methotrexate concentrations within two standard deviations of the mean methotrexate excretion curve specific for the dose of methotrexate administered) or those with normal or mildly impaired renal function because of the potential risk of subtherapeutic exposure to methotrexate.

### Authorization

An approved *Treatment Authorization Request* (TAR) is required for reimbursement. Clinical information submitted with the TAR must confirm that the drug is being used only for the indication above and is in agreement with the stated limitation of use.

### Dosage

A single intravenous injection of 50 units per kg.

### Billing

HCPCS code C9293 (injection, glucarpidase, 10 units).

## Golimumab (Intravenous)

Golimumab is a human IgG monoclonal antibody specific for human tumor necrosis factor (TNF) alpha, and binds to both the soluble and transmembrane bioactive forms of human TNF alpha. Elevated TNF alpha levels in the blood, synovium and joints have been implicated in the pathophysiology of rheumatoid arthritis (RA). TNF alpha is an important mediator of the articular inflammation that is characteristic of RA. The binding of golimumab to TNF alpha prevents the binding of TNF alpha to its receptors, thereby inhibiting its biological activity.

### Indications

Golimumab, in combination with methothetrexate, is indicated for adult patients 18 years of age and older with moderate to severely active RA.

### Authorization

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

### Dosage

The recommended dose is 2 mg/kg given as an intravenous infusion over 30 minutes at weeks zero and four, then every eight weeks.

## Billing

HCPCS code J1602 (injection, golimumab, 1 mg).

One (1) billed unit equals the entire dose administered.

# Golodirsen (VYONDYS 53™)

Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping.

## Indications

All FDA-approved indications

## Dosage

FDA-approved dosages

## TAR/SAR Requirement

An approved *Treatment Authorization Request* (TAR) or CCS Program *Service Authorization Request* (SAR) is required for reimbursement.

## TAR/SAR Criteria

A. Initial Authorization

Golodirsen is both a Medi-Cal and CCS Program benefit when the following criteria are met:

1. Must be for FDA-approved indications and dosages
2. Patient must be 6 years of age or older
3. Patient has documented Duchenne muscular dystrophy (DMD) with dystrophin gene mutation, amenable to exon 53 skipping documented by genetic test(s).
4. Care is under the supervision and monitoring of a neurologist, or for CCS patients, a CCS-paneled neurologist or physical medicine and rehabilitation specialist at a CCS Neuromuscular Medicine Special Care Center (SCC).

5. Documentation of the following information must be provided and for CCS patients, CCS Neuromuscular Medicine SCC or neurology center has provided the following information using the Antisense Oligonucleotide Request Form:
   a) Documentation of percent forced vital capacity (FVC) ≥ 30 percent
   b) Baseline 6-minute walk test (6MWT) or explanation of why the test cannot be performed
6. Patient is on a corticosteroid or has documented reason not to be on this medication
7. Patient is ambulatory

**Initial authorization is for six months**

B. Reauthorization

Golodirsen shall be reauthorized for up to one year when the initial coverage criteria are met, in addition to the following:

1. Patient has not had significant decline in FVC while on the antisense oligonucleotide treatment.
2. Motor function has improved compared to pretreatment assessment as evidenced by improved score in 6MWT, Brooke Score and/or other standardized assessment of motor function, or quantifiable description of improvement by the physician or physical therapist in the medical record.
3. Patient has not experienced significant adverse effects attributable to golodirsen.

C. Patients with percent FVC less than 30 percent and Brooke Score of six may not be granted TAR/SAR authorizations because at the time of this policy, there is insufficient evidence of efficacy in that population.

D. Additional consideration for medical necessity determination. For clients who do not meet the criteria described in sections A. or B above, SCCs may also submit other clinical documentation and/or evidence that would support the medical necessity for initial or reauthorization of the client's antisense oligonucleotide treatments. SCCs should submit this documentation to the Integrated Systems of Care Division (ISCD) Medical Director or designee

I. Policy Implementation for CCS Patients

A. Submission of authorization requests for golodirsen are not included in Service Code Groupings (SCGs). SCCs should submit a separate Service Authorization Request (SAR) with the following documentation: a copy of the prescription, genetic laboratory test result with specific mutation, clinical progress notes from a visit within the past 6 months, and a copy of Antisense Oligonucleotide Request Form.

1. For patients residing in an independent county, SARs should be submitted to the CCS independent county office, which shall review and authorize according to the policy above.
2. For patients residing in a dependent county, SARs should be submitted to dependent county office. The dependent county program office shall pend and submit the SAR and Antisense Oligonucleotide Request Form to the Department of Health Care Services (DHCS) ISCD Special Populations Authorization Unit e-mail at CCSOperations@dhcs.ca.gov or via secure RightFax at (916) 440-5768.

B. All antisense oligonucleotide requests shall be reviewed by a CCS Program Medical Director or designee before authorization. If you have any questions regarding benefit for CCS patients, please contact the ISCD Medical Director or designee, via e-mail at ISCD-MedicalPolicy@dhcs.ca.gov.

### Age Limits

Must be 6 years of age or older

### Billing

HCPCS code J1429 (injection, golodirsen, 10 mg)

### Suggested ICD-10 Diagnosis Codes

G71.01

### Prescribing Restrictions

Frequency of billing equals 30 mg/kg once weekly

## Granisetron

Granisetron is a selective 5-hydroxytryptamine3 (5-HT3) receptor antagonist with little or no affinity for other serotonin receptors.

### Indications

Granisetron injection is indicated for:

- The prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy.
- The prevention and treatment of postoperative nausea and vomiting in adults. As with other antiemetics, routine prophylaxis is not recommended in patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and/or vomiting must be avoided during the postoperative period granisetron injection is recommended even where the incidence of postoperative nausea and/or vomiting is low.

## Dosage

For the prevention of chemotherapy-induced nausea and vomiting, the recommended dosage for granisetron injection is 10 mcg/kg administered intravenously within 30 minutes before initiation of chemotherapy, and only on the day(s) chemotherapy is given. Medical justification is required when the dosage exceeds 1,400 mcg.

For the prevention of postoperative nausea and vomiting, the recommended dosage is 1,000 mcg of granisetron, undiluted, administered intravenously over 30 seconds, before induction of anesthesia or immediately before reversal of anesthesia. The recommended dosage for the treatment of nausea and/or vomiting after surgery is 1,000 mcg of granisetron undiluted, administered intravenously over 30 seconds.

## Billing

HCPCS code J1626 (injection, granisetron HCl, 100 mcg).

# Granisetron Extended Release

Granisetron extended release injection is a serotonin-3 (5-HT3) receptor antagonist with little or no affinity for other serotonin receptors. Serotonin receptors of the 5-HT3 type are located peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postrema. During chemotherapy-induced vomiting, mucosal enterochromaffin cells release serotonin, which stimulates 5-HT3 receptors. This evokes vagal afferent discharge and may induce vomiting.

## Indications

Prevention of nausea and/or vomiting associated with the initial and repeat courses of emetogenic cancer therapy, postoperative, anesthesia.

## Dosage

For the prevention of chemotherapy-induced nausea and vomiting the recommended dosage is:

- Patients (17 years of age and older) 10 mcg/kg intravenously within 30 minutes before initiation of chemotherapy.
- Pediatric patients (2 thru 16 years of age) 10 mcg/kg.

For the prevention of postoperative nausea and vomiting, the recommended dosage is:

1 mg, undiluted, administered intravenously over 30 seconds, before anesthetic induction or immediately before reversal of anesthesia

For the treatment of postoperative nausea and vomiting, the recommended dosage is:

1 mg, undiluted, administered intravenously over 30 seconds.

## Authorization

An approved TAR is required for reimbursement. The TAR must state that the treatment is for a patient with nausea and/or vomiting associated with cancer treatment.

## Required Codes

ICD-10-CM diagnosis codes: K91.0, R11.0, R11.2, Z51.11 and Z98.890

## Billing

HCPCS code J1627 (injection, granisetron extended release, 0.1 mg).

# Granisetron HCL

Granisetron is a selective 5-hydroxytryptamine3 (5-$HT_3$) receptor antagonist with little or no affinity for other serotonin receptors.

## Indications

Granisetron injection is indicated for:

- The prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy.
- The prevention and treatment of postoperative nausea and vomiting in adults. As with other antiemetics, routine prophylaxis is not recommended in patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and/or vomiting must be avoided during the postoperative period granisetron injection is recommended even where the incidence of postoperative nausea and/or vomiting is low.

## Dosage

For the prevention of chemotherapy-induced nausea and vomiting, the recommended dosage for granisetron injection is 10 mcg/kg administered intravenously within 30 minutes before initiation of chemotherapy, and only on the day(s) chemotherapy is given. Medical justification is required when the dosage exceeds 1,400 mcg.

For the prevention of postoperative nausea and vomiting, the recommended dosage is 1,000 mcg of granisetron, undiluted, administered intravenously over 30 seconds, before induction of anesthesia or immediately before reversal of anesthesia. The recommended dosage for the treatment of nausea and/or vomiting after surgery is 1,000 mcg of granisetron undiluted, administered intravenously over 30 seconds.

### Billing

HCPCS code J1626 (injection, granisetron HCl, 100 mcg).

## Growth Hormone Injections

For information about the use of growth hormone injections for HIV-associated wasting, see "Somatropin for HIV-Associated Wasting" in the Injections: *Drugs S – Z* Policy section in this manual.

## Guselkumab

Guselkumab is an interleukin-23 blocker solution for subcutaneous (SQ) use.

### Indications

Guselkumab injection is used for the treatment of moderate-to-severe chronic plaque psoriasis (i.e. extensive and/or disabling disease) who are candidates for systemic therapy or phototherapy and when other systemic therapies are medically less appropriate.

### Age

18 years and older

### Dosage

The recommended dose is 100 mg SQ injection administered at weeks 0 and 4, and every 8 weeks thereafter.

### 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, conventional therapy has been tried or considered, has failed, or is contra-indicated.
- The physician's legible, complete, and signed treatment plan/order for guselkumab.

### Billing

HCPCS code J1628 (injection, guselkumab, 1 mg)

One (1) unit of J1628 equals 1 mg of guselkumab solution

# Hemin

Hemin, 1 mg, (HCPCS code J1640) is reimbursable for females 10 years of age or older. It may be reimbursed up to a maximum of 602 mg.

# Histrelin Acetate

Histrelin acetate, 10 mcg, (HCPCS injection code J1675) is reimbursable with authorization, for patients with precocious puberty. Claims must be billed "By Report" and shall include an invoice for the kit.

# Histrelin Acetate Implant

For information regarding HCPCS code J9226 (histrelin acetate implant [Supprelin® LA] 50 mg) and HCPCS code J9225 (histrelin implant [Vantas®] 50 mg), see the *Non-Injectable Drugs* section in the appropriate Part 2 manual.

# Human Fibrinogen Concentrate

Human fibrinogen concentrate is used in treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

## Dosage

The usual maximum dosage is 7,000 mg (quantity of 70) per day. Claims billed for greater quantities require documentation that patient's weight exceeds 100 kg.

## Required Diagnosis Code

Restricted to ICD-10-CM diagnosis code D68.2.

## Billing

HCPCS code J7178 (injection, human fibrinogen concentrate, not otherwise specified, 1 mg).

One unit equals 1 mg

# Hyaluronan

Hyaluronan for intra-articular injection is reimbursable for the treatment of osteoarthritis of the knees.

## Authorization

An approved *Treatment Authorization Request* (TAR) is required for reimbursement. Documentation must include all of the following:

- Painful osteoarthritis of one or both knees
- Inadequate response to conservative nonpharmacologic therapy
- Inadequate response to analgesics (for example, acetaminophen) and non-steroidal anti-inflammatory drugs

## Billing

HCPCS code J7324 (hyaluronan or derivative, Orthovisc®, for intra-articular injection per dose).

HCPCS code J7326 (hyaluronan or derivative, GelOne®, for intra-articular injection, per dose).

HCPCS code J7327 (hyaluronan or derivative, Monovisc®, for intra-articular injection, per dose).

HCPCS code J7328 (hyaluronan or derivative, Gel-Syn®, for intra-articular injection, 0.1 mg), must be billed “By Report”

# Hyaluronan or Derivative Injections (Durolane, Hyalgan, Supartz, Visco-3, Euflexxa, Synojoynt and Triluron)

Hyaluronan or derivatives are injected directly into a patient's knee for relief of pain associated with osteoarthritis. They are used for the replacement or supplementation of naturally occurring intra-articular lubricants in individuals with musculoskeletal conditions. They may work by acting as a lubricant and shock absorber in the joint, helping the knee to move smoothly, thereby lessening pain.

## Indications

All FDA-approved indications

## Dosage

FDA-approved dosages

## TAR Requirement

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

## TAR Criteria

A hyaluronan derivative intra-articular injection is considered medically necessary when all of the following criteria are met:

- Prescribed for FDA-approved indications and dosing regimens
- Patient must be 18 years of age or older (Triluron, Hyalgan, Supartz, Euflexxa) and 22 years of age or older (Synojoynt and Durolane and Visco-3)
- Must have documented clinical diagnosis of osteoarthritis of the knee
- Must have documented failure, inadequate response, or intolerance to at least two of the following pharmacologic therapies
  - Two oral or topical [e.g., oral non-steroidal anti-inflammatory drugs (NSAIDs), COX-2 inhibitors, or topical NSAIDS (e.g. diclofenac 1 percent gel)]
  - Acetaminophen
  - One or more trials in the last 12 months of intra-articular steroid injections unless intolerant or contraindicated
- At least one course of physical therapy for knee osteoarthritis

- No contraindications to the injections (active joint infection, bleeding disorder)
- Patient must be treated with the less expensive but clinically appropriate hyaluronan derivatives first

**For treatment continuation, the following criteria must be met:**

- Patient has successfully used hyaluronic acid derivatives in the same knee (there must be at least a six-month interval before approval of a repeat course)

## Age Limit

Synojoynt, Durolane and Visco-3: Must be 22 years of age or older

Triluron, Hyalgan, Supartz and Euflexxa: Must be 18 years of age or older

## Billing

Durolane: HCPCS code J7318 (hyaluronan or derivative, durolane, for intra-articular injection, 1 mg)

Hyalgan/Supartz/Visco-3: HCPCS code J7321 (Hyaluronan or derivative, hyalgan, supartz, or visco-3 for intra-articular injection, per dose)

Euflexxa: HCPCS code J7323 (hyaluronan or derivative, euflexxa, for intra-articular injection, per dose)

Synojoynt: HCPCS code J7331 (hyaluranon or derivative, synojoynt, for intra-articular injection, 1 mg)

Triluron: HCPCS code J7332 (hyaluranon or derivative, triluron, for intra-articular injection, 1 mg)

Must use modifiers RT, LT for applicable knee(s)

**Prescribing Restrictions**

| Product | Package Size | Dosage and Administration (per knee per 180 days) | Maximum billing units (per knee per 180 days) |
|---|---|---|---|
| Durolane | 60 mg/ml | 60 mg intra-articularly x 1 administration | 60 units |
| Euflexxa | 20 mg/2 ml | 20 mg intra-articularly once weekly x 3 administrations | 3 units |
| Hyalgan | 20 mg/2 ml | 20 mg intra-articularly once weekly x 3-5 administrations | 5 units |
| Supartz | 25 mg/ 2.5 ml | 25 mg intra-articularly once weekly x 3-5 administrations | 5 units |
| Synojoynt | 20 mg/2 ml | 20 mg intra-articularly once weekly x 3 administrations | 60 units |
| Triluron | 20 mg/2 ml | 20 mg intra-articularly once weekly x 3 administrations | 60 units |
| Visco-3 | 25 mg/2.5 ml | 25 mg intra-articularly once weekly for 3 administrations | 3 units |

## Hydroxyprogesterone Caproate

Policy information about hydroxyprogesterone caproate can be located under “Preventing Preterm Births: Hydroxyprogesterone Caproate” in the *Pregnancy: Early Care and Diagnostic Services* section of the appropriate Part 2 manual. Use the following codes when billing for hydroxyprogesterone caproate:

- HCPCS code J1726 (Makena)
- HCPCS code J1729 (not otherwise specified)
- HCPCS code J3490 (unclassified drug), if billing for a compounded version

# Hylan G-F 20

Hylan G-F 20 for intra-articular injection is reimbursable for treatment of the knees. Authorization is required and documentation must be submitted with the *Treatment Authorization Request* (TAR) that satisfies all of the following conditions:

- Painful osteoarthritis of one or both knees
- Inadequate response to conservative nonpharmacologic therapy
- Inadequate response to analgesics (for example, acetaminophen) and non-steroidal anti-inflammatory drugs

The TAR should state which form of Hylan G-F 20 the patient will receive, either Synvisc® or Synvisc-One®.

## Dosage

Hylan G-F 20 (Synvisc): The usual dose is 16 mg into the affected knee at weekly intervals for three weeks for a total of three injections per affected knee.

Hylan G-F 20 (Synvisc-One): The usual dose is 48 mg into the affected knee. Synvisc-One combines three doses of Synvisc into a single syringe.

Providers may administer more than 48 units of Hylan G-F 20 (Synvisc-One) per day if bilateral knee injections are needed on the same day.

## Billing

HCPCS code J7325 (hyaluranon or derivative, Synvisc or Synvisc-One, for intra-articular injection, 1 mg).

When billing for Synvisc or Synvisc-One, one billing unit is equivalent to 1 mg.

# Hymovis®

Hymovis is a sterile, non-pyrogenic, viscoelastic hydrogel contained in a single-use syringe. Hymovis is based on an ultra-pure hyaluronan, engineered using a proprietary process to increase viscosity, elasticity and residence time without chemical crosslinking. This results in a natural hyaluronan similar to the hyaluronan found in the synovial fluid present in the human joint.

## Indication

Hymovis is indicated for the treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative, non-pharmacologic therapy and simple analgesics, such as acetaminophen.

## Dosage

Hymovis is administered by intra-articular injection. A treatment cycle consists of two injections given a week apart. Strict aseptic administration technique must be followed. Inject the full 3 ml in one knee only. Do not overfill the joint. If treatment is bilateral, a separate syringe should be used for each knee.

## Required Codes

CD-10-CM diagnosis codes:

| | | |
|---|---|---|
| M17.0 | M17.2 | M17.4 |
| M17.10 | M17.30 | M17.5 |
| M17.11 | M17.31 | M17.9 |
| M17.12 | M17.32 | |

## Billing

HCPCS code J7322 (hyaluronan or derivative, hymovis, for intra-articular injection, 1 mg)

## 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. |