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 equals 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 two 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 greater than or equal to six
  - 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 two 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 equal 1 mg of edaravone injection solution

‹‹Efgartigimod alfa-fcab (Vyvgart™)

Efgartigimod alfa-fcab is a human Immunoglobulin G1 (IgG1) antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating immunoglobulin G (IgG).

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following:

- 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 a neurologist
- Patient has a diagnosis of Myasthenia Gravis (MG) with generalized muscle weakness
- Patient meets the criteria of Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV
- Patient has a positive serological test for anti-AChR antibodies››

- ‹‹Patient has MG-Activities of Daily Living (MG-ADL) total score of at least five (greater than 50 percent non-ocular)
- Documentation of total Quantitative Myasthenia Gravis (QMG) score
- Patient is on standard-of-care such as acetylcholinesterase (AChE) inhibitors, steroids and immunosuppressant agents (e.g., azathioprine, methotrexate, cyclosporine, tacrolimus, mycophenolate mofetil, and cyclophosphamide), either alone or in combination
  - If not on standard-of-care, must have had adequate trial of AchE and at least two immunosuppressant agents with clinical justification why patient is not on them, such as treatment failure, allergy, intolerance, contraindication, etc.

Initial authorization is for six months

Continued therapy

- Patient continues to meet initial approval criteria
- Patient has shown clinical benefit as shown by one of the following:
  - Two-point or greater reduction in the total MG-ADL score as compared to baseline.
  - A reduction of at least three points on the total (QMG) score from baseline
  - Documented reduction in symptoms that impact daily function

Reauthorization is for 12 months

Age Limits

Must be 18 years of age or older

Billing

HCPCS code J9332 (injection, efgartigimod alfa-fcab, 2mg)

Required ICD-10 Diagnosis Codes

G70.00, G70.01

Prescribing Restriction(s)

Frequency of billing equals 10 mg/kg once weekly for four weeks

Maximum billing unit(s) equals 1200 mg/600 units››

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) greater than or equal to 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 one to ten mg/kg/dose two 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 equals 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 (Fabrazyme®)
- Alglucosidase Alfa (Lumizyme®)
- Avalglucosidase alfa-ngpt (Nexviazyme)
- Cerliponase Alfa (Brineura)
- Elosulfase Alfa (Vimizim®)
- Galsulfase (Naglazyme®)
- Idursulfase (Elaprase®
- Imiglucerase (Cerezyme)
- Laronidase (Aldurazyme®)
- Olipudase Alfa-rpcp (Xenpozyme)
- Velaglucerase Alfa (Vpriv)
- Vestronidase Alfa-vjbk (Mepsevii™)

Specific authorization and billing requirements are listed for each enzyme replacement drug.

Medical providers to note that *Treatment Authorization Requests* (TARs) for Enzymes Replacement Drugs which are purchased by providers and billed as a medical benefit ("buy and bill"), should continue to be submitted to TAR Processing Center same as other "medical" TARs for fee-for-service (FFS) beneficiaries. For Medi-Cal managed care plan enrollees, provider should contact the individual plan for prior authorization and billing instructions.

Agalsidase beta (Fabrazyme®)

Fabrazyme (agalsidase beta) provides an exogenous source of α-galactosidase A in Fabry disease patients. Agalsidase beta is internalized and transported into lysosomes where it exerts enzymatic activity and reduces accumulated GL-3.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following:

- Must be used for FDA-approved indications and dosages
- Patient must be two years of age or older
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders.
- Patient has a diagnosis of Fabry's disease confirmed by one of the following:
  - Genetic determination of the galactosidase alpha (GLA) or alpha-Gal A mutations
  - Leukocyte alpha-galactosidase A (alpha-Gal A) activity (less than 3 percent) in males
  - Presence of Globotriaosylceramide (Gb3) and globotriaosylsphingosine (lysoGb3) in the plasma and urine
- Clinical presentation consistent with Fabry's disease (for example, angiokeratomas, telangiectasias, hypohidrosis or anhydrosis, corneal opacities, edema or lymphedema, abnormal cardiac examination (evidence of left ventricular hypertrophy [LVH], arrhythmias, etc)

- Documentation of plasma GL-3 and/or GL-3 inclusions at baseline

Initial authorization is for six months

Continued treatment

- Patient continues to meet initial approval criteria
- Patient has experienced positive clinical response as evidenced by:
  - Reduction in plasma GL-3 levels from baseline
  - Reduction of GL-3 inclusions from baseline
  - Stabilization or improvement in in renal function, pain reduction from baseline

Reauthorization is for 12 months

Age Limits

Must be two years of age or older

Billing

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

Suggested ICD-10-CM Diagnosis Codes

E75.21

Prescribing Restrictions

Frequency of billing equals 1 mg/kg body weight given every two weeks

Alglucosidase alfa (Lumizyme®)

Pompe disease (acid maltase deficiency, glycogen storage disease type II, GSD II, glycogenosis type II) is an inherited disorder of glycogen metabolism caused by the absence or marked deficiency of the lysosomal enzyme GAA.

Alglucosidase alfa provides an exogenous source of GAA. Binding to Mannose-6-Phosphate receptors on the cell surface has been shown to occur via carbohydrate groups on the GAA molecule, after which it is internalized and transported into lysosomes, where it undergoes proteolytic cleavage that results in increased enzymatic activity. It then exerts enzymatic activity in cleaving glycogen.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation that demonstrates the following:

Universal criteria

- Must be used for FDA-approved indications and dosages.
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders.
- Patient has documented baseline results of Forced Vital Capacity (FVC) and/or six Minute Walk Test (6MWT) or motor function such as Alberta Infant Motor Scale (AIMS).
- Patient is not concurrently taking Avalglucosidase Alfa-ngpt (Nexviazyme™)

Infantile-onset Pompe disease

- Patient has a diagnosis of infantile-onset Pompe disease confirmed by one of the following:
  - Genetic testing for deletion or mutations in the GAA gene
  - Measurement of alpha-glucosidase activity in cultured amniocytes or chorionic villus samples
- Patient has clinical signs and symptoms of the disease (for example: cardiomegaly, respiratory distress, muscle weakness, feeding difficulties, failure to thrive, etc.)

Late-onset Pompe disease

- Patient has a diagnosis of late-onset Pompe disease confirmed by one or both of the following:
  - Enzyme assay from any tissue source (for example skin fibroblast or muscle) demonstrating lysosomal acid alpha-glucosidase (GAA) enzyme deficiency
  - Genetic testing with two confirmed GAA gene variants
- Patient has one or more clinical signs and symptoms of the disease (for example: skeletal myopathy, respiratory distress, delayed gross-motor development and progressive weakness, etc.)

Initial authorization is for six months.

Continued therapy

- Patient continues to meet initial approval criteria.
- Patient has shown clinical benefit as evidenced by at least one of the following:
  - Change in FVC (percent predicted) from baseline
  - Change in total distance walked in six minutes (six Minute Walk Test, [6MWT]) from baseline
  - Improvement in cardiac function from baseline such as decrease in left ventricular mass index (LVMI)
  - Gains in motor function assessed by the Alberta Infant Motor Scale (AIMS) or other standard scale

Reauthorization is for 12 months.

Billing

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

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

Suggested ICD-10-CM Diagnosis Codes

E74.02

Prescribing Restrictions

Frequency of billing equals 20 mg per kg body weight administered every two weeks.

Avalglucosidase Alfa-ngpt (Nexviazyme™)

Pompe disease (also known as glycogen storage disease type II, acid maltase deficiency, and glycogenosis type II) is an inherited disorder of glycogen metabolism caused by a deficiency of the lysosomal enzyme acid α-glucosidase (GAA), which results in intralysosomal accumulation of glycogen in various tissues.

Avalglucosidase alfa-ngpt provides an exogenous source of GAA. The Mannose-6-phosphate (M6P) on avalglucosidase alfa-ngpt mediates binding to M6P receptors on the cell surface with high affinity. After binding, it is internalized and transported into lysosomes where it undergoes proteolytic cleavage that results in increased GAA enzymatic activity. Avalglucosidase alfa-ngpt then exerts enzymatic activity in cleaving glycogen.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

TheTAR must include clinical documentation that demonstrates the following:

- Must be used for FDA-approved indications and dosages.
- Patient must be one year of age or older
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders.
- Patient must have a diagnosis of late-onset Pompe disease confirmed by at least one of the following:
  - *Enzyme assay from* any tissue source(for example skin fibroblast or muscle) demonstrating lysosomal acid alpha-glucosidase (GAA) enzyme deficiency.
  - Genetic testing with two confirmed GAA gene variants
- Patient has documented baseline results of Forced Vital Capacity (FVC) and/or six Minute Walk Test (6MWT)
- Patient is not concurrently taking Alglucosidase Alfa (Lumizyme)

Initial authorization is for six months

Continued therapy

- Patient continues to meet initial approval criteria
- Patient has shown clinical benefit as evidenced by at least one of the following:
  - Change in FVC (percent predicted) in the upright position from baseline
  - Change in total distance walked in six minutes (six Minute Walk Test, [6MWT]) from baseline.

Reauthorization is for 12 months.

Age Limits

Must be one year of age or older

Billing

HCPCS code J0219 (injection, avalglucosidase alfa-ngpt, 4 mg)

Suggested ICD-10-CM Diagnosis Codes

E74.02

Prescribing Restrictions

Frequency of billing:

- Greater than or equal to 30 kg, 20 mg/kg (of actual body weight) every two weeks
- Less than 30 kg, 40 mg/kg (of actual body weight) every two weeks

Cerliponase alfa (Brineura®)

Ceroid lipofuscinosis type 2 (CLN2) disease is a neurodegenerative disease caused by deficiency of the lysosomal enzyme tripeptidyl peptidase-1 (TPP1), which catabolizes polypeptides in the CNS. TPP1 has no known substrate specificity. Deficiency in TPP1 activity results in the accumulation of lysosomal storage materials normally metabolized by this enzyme in the central nervous system (CNS), leading to progressive decline in motor function.

Cerliponase alfa (rhTTP1), a proenzyme, is taken up by target cells in the CNS and is translocated to the lysosomes through the Cation Independent Mannose-6-Phosphate Receptor (CI-MPR, also known as M6P/IGF2 receptor). Cerliponase alfa is activated in the lysosome and the activated proteolytic form of rhTPP1 cleaves tripeptides from the N-terminus of proteins.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation that demonstrates the following**:**

- Must be used for FDA-approved indications and dosages
- Patient must be three years of age or older
- Must be prescribed by or in consultation with a neurologist, geneticist or other physician with specialty in treating CLN2 disease
- Patient must have a diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency confirmed by one of the following:
  - Enzyme assay with a deficiency of TPP1 enzyme activity
  - Genetic testing showing mutation of the TPP1 gene
- Patient does not have any acute intraventricular access device-related complication (for example: leakage, extravasation of fluid, or device failure) or ventriculoperitoneal shunts.
- Patient has a documentation of mild to moderate disease with a two-domain score of three to six on motor and language domains of the Hamburg CLN2 Clinical Rating Scale, with a score of at least 1 in each domain.
- Patient is ambulatory at the time of treatment initiation.

Initial authorization is for six months.

Continued therapy

- Patient continues to meet initial approval criteria.
- Patient has shown positive clinical response as evidenced by a slowed loss of ambulation or motor deterioration (for example, crawling ability or walking) from baseline; OR has at least a 1 on the Motor domain of the Hamburg CLN2 Clinical Rating Scale.
- Patient does not have acute intraventricular access device-related complications (for example: leakage, device failure, or device-related infection) or ventriculoperitoneal shunts.

Reauthorization is for 12 months

Age Limits

Must be three years of age or older

Billing

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

Required ICD-10-CM Diagnosis Codes

E75.4

Prescribing Restrictions

Frequency of billing equals 300 mg/300 units once every other week

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

Elosulfase alfa (Vimizim®)

Elosulfase alfa is a recombinant form of N-acetylgalactosamine-6-sulfatase, produced in Chinese hamster cells. A deficiency of this enzyme leads to accumulation of the glycosaminoglycan (GAG) substrates (keratan sulfate and chondroitin-6-sulfate) in tissues, causing cellular, tissue and organ dysfunction. Elosulfase alfa provides the exogenous enzyme (N-acetylgalactosamine-6-sulfatase) that is taken into lysosomes and thereby increases the catabolism of the GAG substrates (for example: keratan sulfate and chondroitin-6-sulfate).

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following:

- Must be used for FDA approved indications and dosages
- Patient must be 5 years of age or older
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders
- Patient must have a clinical diagnosis of MPS IV A (Morquio A syndrome) based on one of the following:
  - Genetic testing identifying mutations in the gene encoding N-acetylgalactosamine-6-sulfatase (galactosamine-6-sulfatase) [GALNS]
  - Enzyme assay showing an absence or low GALNS activity
- Patient has a documentation of one or more clinical signs and symptoms of MPS IV A: For example, skeletal disease with short stature, knee deformities, scoliosis/kyphosis, knock-knee deformity, hip dysplasia, arthralgia, corneal opacities, hearing loss, etc.
- Patient must have an average screening 6MWT distance greater than or equal to 30 and less than or equal to 325 meters
- Patient does not have a known hypersensitivity to any of the components of elosulfase alfa

Initial authorization is for six months.

Continued therapy:

- Patient continues to meet initial approval criteria
- Patient has shown clinical benefit as evidenced by at least one of the following:
  - Change in total distance walked in six minutes (six Minute Walk Test, [6MWT]) from baseline
  - Change from baseline in urine keratan sulfate (KS) levels
  - Documented improvement from baseline in other parameters such as respiratory function, bone and cartilage metabolism biomarkers, quality of life, cardiac valve function, and corneal clouding

Reauthorization is for 12 months.

Age Limits

Must be five years of age or older

Billing

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

Suggested ICD-10-CM Diagnosis Codes

E76.210

Prescribing Restrictions

Frequency of billing equals two mg per kg once every week

Galsulfase (Naglazyme®)

Mucopolysaccharide storage disorders are caused by the deficiency of specific lysosomal enzymes required for the catabolism of GAG. MPS VI is characterized by the absence or marked reduction in N–acetylgalactosamine 4-sulfatase. The sulfatase activity deficiency results in the accumulation of the GAG substrate, dermatan sulfate, throughout the body. This accumulation leads to widespread cellular, tissue, and organ dysfunction. Naglazyme is intended to provide an exogenous enzyme that will be taken up into lysosomes and increase the catabolism of GAG. Galsulfase uptake by cells into lysosomes is most likely mediated by the binding of mannose-6-phosphate-terminated oligosaccharide chains of galsulfase to specific mannose-6-phosphate receptors.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following:

- Must be used for FDA approved indications and dosages
- Patient must be 5 years of age or older
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders
- Patient must have a clinical diagnosis of MPS VI (Maroteaux-Lamy syndrome) as shown by at least one of the following:
  - Enzyme assay showing leukocyte ASB enzyme activity less than 10 percent of the lower limit of normal
  - Genetic testing with mutations in the gene encoding arylsulfatase B (ARSB, N-acetylgalactosamine 4-sulfatase)
- Patient has documentation of one or more clinical features of disease: For example, coarse facial features, short stature, dysostosis multiplex and degenerative joint disease, elevated urinary glycosaminoglycans (uGAGs), cardiac valve disease, reduced pulmonary function, hepatosplenomegaly, corneal clouding, carpal tunnel disease, inguinal or umbilical hernia, etc.
- Documentation of baseline 12-minute walk test

Initial authorization is for six months.

Continued therapy:

- Patient continues to meet initial approval criteria
- Patient has shown clinical benefit as evidenced by disease improvement or lack of disease progression by at least one of the following:
  - Improvement or stabilization of motor function such as total distance walked in a 12-minute walk test (12-MWT) or number of stairs climbed in a three-minute stair climb test from baseline, or other documented improvement in motor function
  - Reduction in uGAGs, dermatan sulfate, and chondroitin 4-sulfate levels from baseline
  - Other documentation of clinical improvement or disease stabilization

Reauthorization is for 12 months.

Age Limits

Must be five years of age or older

Billing

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

Suggested ICD-10-CM Diagnosis Codes

E76.29

Prescribing Restrictions

Frequency of billing equals 1 mg per kg once weekly

Idursulfase (Elaprase®)

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-O-sulfate moieties from the glycosaminoglycans (GAG) dermatan sulfate and heparan sulfate. Due to the missing or defective iduronate-2-sulfatase enzyme in patients with Hunter syndrome, GAG progressively accumulate in the lysosomes of a variety of cells, leading to cellular engorgement, organomegaly, tissue destruction, and organ system dysfunction.

Elaprase is intended to provide exogenous enzyme for uptake into cellular lysosomes. Mannose-6-Phosphate (M6P) residues on the oligosaccharide chains allow binding of the enzyme to the M6P receptors on the cell surface, leading to cellular internalization of the enzyme, targeting to intracellular lysosomes and subsequent catabolism of accumulated GAG.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation that demonstrates the following**:**

- Must be used for FDA-approved indications and dosages
- Patient must be male, 16 months of age or older
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders
- Patient must have a diagnosis of Mucopolysaccharidosis Type II (MPS II or Hunter syndrome)
- Diagnosis is confirmed by one of the following:
  - Enzyme assay showing a deficiency in iduronate-2-sulfatase (I2S) enzyme activity in plasma, fibroblasts or leukocytes and/or a normal enzyme activity level of one other sulfatase (based on normal range of measuring laboratory)
  - Genetic testing showing pathogenic mutations in the IDS gene
- Patient has documentation of one or more clinical features of disease: hepatosplenomegaly, radiographic evidence of dysostosis multiplex, valvular heart disease, evidence of obstructive pulmonary disease etc.
- Documentation of baseline forced vital capacity (less than 80% of predicted normal value)
- Documentation of urinary GAG levels at baseline

Initial authorization is for six months

Continued therapy

- Patient continues to meet the Initial approval criteria
- Patient has shown positive clinical response to therapy from baseline as evidenced by at least one of the following:
  - Change from baseline in distance walked in six minutes (six minute walk test)
  - Reduction in mean urinary GAG levels from baseline
  - Reduction in both liver and spleen volumes from baseline
  - Improvement or stabilization in FVC

Reauthorization is for 12 months

Age Limits

Must be 16 months or older

Billing

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

Suggested ICD-10-CM Diagnosis Codes

E76.1

Prescribing Restrictions

Frequency of billing equals 0.5 mg per kg once every week

Imiglucerase (Cerezyme®)

Gaucher disease is characterized by a deficiency of β-glucocerebrosidase activity, which results in accumulation of glucocerebroside in various tissues including liver, spleen, and bone marrow. The mannose sugars on imiglucerase mediate binding to and internalization by cells including macrophages. Cerezyme catalyzes the hydrolysis of glucocerebroside to glucose and ceramide.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation that demonstrates the following:

- Must be used for FDA-approved indications and dosages
- Patient must be two years of age or older
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders
- Patient has a diagnosis of Gaucher disease type 1 diagnosed confirmed by one of the following:
  - Enzyme analysis identifying deficiency of β-glucocerebrosidase activity
  - DNA analysis to identify genetic mutation

- Patient has at least one of the following:
  - Hemoglobin value of greater than or equal to 11.0 g/dL for women and greater than or equal to 12.0 g/dL for men
  - Splenomegaly, hepatomegaly
  - Thrombocytopenia (platelet count less than 100,000/mm^3)
  - Disease symptoms such as fatigue, growth retardation, osteopenia/osteoporosis, bony abnormalities and bone pain

Initial authorization is for six months

Continued therapy

- Patient continues to meet initial approval criteria
- Patient has shown positive clinical response as evidenced by at least one of the following changes from baseline:
  - Increase in hemoglobin concentration of at least 1 g/dl
  - Increase in platelet count
  - Decrease in spleen and/or liver volume
  - Bone x-rays showing improvements in cortical thickness and lucencies
  - Reduced bone pain and or/fatigue, or bruising and bleeding

Reauthorization is for 12 months

Age Limits

Must be two years of age or older

Billing

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

Suggested ICD-10-CM Diagnosis Codes

E75.22

Prescribing Restrictions

Frequency of billing equals 2.5 units/kg three times a week to sixty units/kg once every two weeks

Billing

HCPCS code J1786 (injection, imiglucerase, per 10 units).

Laronidase (Aldurazyme®)

Laronidase is a recombinant (replacement) form of alpha-L-iduronidase derived from Chinese hamster cells. Alpha-L-iduronidase is an enzyme needed to break down endogenous glycosaminoglycans (GAGs) within lysosomes. A deficiency of alpha-L-iduronidase leads to an accumulation of GAGs, causing cellular, tissue, and organ dysfunction as seen in Mucopolysaccharidosis I (MPS I). Improved pulmonary function and walking capacity have been demonstrated with the administration of laronidase to patients with Hurler, Hurler-Scheie, or Scheie (with moderate-to-severe symptoms) forms of MPS.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following

- Must be used for FDA approved indications and dosages
- Patient must be six months or older
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders.
- Patient must have a diagnosis of MPS I confirmed by one of the following clinical and enzymatic assessments:
  - Enzyme assay demonstrating deficiency in alpha-L-iduronidase activity
  - Genetic testing confirming mutations in the alpha-L-iduronidase gene
- Patient has one of the following MPS1 clinical phenotypes of varying severity:
  - Hurler syndrome (MPS IH); severe
  - Hurler-Scheie Syndrome (MPS IH-S); intermediate
  - Scheie Syndrome (MPS IS); mild

- Patient has documentation of one or more of the following:
  - Enlarged liver or spleen size (equals one and a half times normal for age)
  - Elevated urinary glycosaminoglycans (uGAG) (equals five times normal for age)
  - A baseline forced vital capacity (FVC) less than or equal to 80% of predicted

Initial approval is for six months

Continuation of therapy

- Patient continues to meet the Initial approval criteria
- Patient has shown positive clinical response to therapy as evidenced by at least one of the following from baseline:
  - Reduction in liver and/or spleen volume
  - Reduction in urinary GAG excretion
  - Improvement in joint stiffness/range of motion
  - Improvement or stabilization in 6-minute walk test (6MWT)
  - Improvement or stabilization in FVC

Reauthorization will be for 12 months

Age Limits

Must be 6 months or older

Billing

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

Suggested ICD-10-CM Diagnosis Codes

E76.01, E76.02, E76.03

Prescribing Restrictions

Frequency of billing equals 0.58 mg/kg once weekly.

‹‹Olipudase Alfa-rpcp (Xenpozyme)

Acid sphingomyelinase deficiency (ASMD) is a lysosomal storage disease that results from reduced activity of the enzyme acid sphingomyelinase (ASM), caused by pathogenic variants in the sphingomyelin phosphodiesterase 1 gene. ASM degrades sphingomyelin to ceramide and phosphocholine. The deficiency of ASM causes an intra-lysosomal accumulation of sphingomyelin (as well as cholesterol and other cell membrane lipids) in various tissues. XENPOZYME provides an exogenous source of ASM. XENPOZYME is not expected to cross the blood-brain barrier or modulate the CNS manifestations of ASMD.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following:

- Must be used for FDA-approved indications and dosages
- Must be prescribed by or in consultation with a specialist familiar with the treatment of lysosomal storage disorders
- Patient has a clinical diagnosis of acid sphingomyelinase deficiency (ASMD) as confirmed by:
  - Genetic testing
  - Enzyme assay showing reduced activity of the enzyme acid sphingomyelinase (ASM)
- Diagnosis consistent with ASMD (Niemann-Pick disease) type B and A/B
- Patient has non-central nervous system (non-CNS) manifestations ASM deficiency
- Patient is not a pregnant or breast-feeding female
- Baseline ALT and AST (within 1 month prior to initiation of therapy; within 72 hours prior to dose escalation; within 72 hours after the end of the infusion if the baseline or preinfusion ALT/AST is more than 2 times ULN; as clinically indicated during maintenance therapy).››

- ‹‹Adult patients (18 years old or older) must have all of the following:
  - Baseline diffusion capacity of the lungs for carbon monoxide (DLco) 70 percent or less of the predicted normal value
  - Spleen volume greater than or equal to 6 multiples of normal (MN) measured by MRI
  - Splenomegaly related score (SRS) are greater than or equal to 5
- Pediatric patients (younger than 18 years old) must have all of the following:
  - Patient did not have delay of gross motor skills
  - Height was -1 Z-score or lower
  - Patient has a spleen volume greater than or equal to 5 MN measured by MRI.

Initial authorization is for 12 months.

Reauthorization

- Patient has shown a positive clinical response as shown by at least one of the following:
  - Increase in percentage predicted DLCO from baseline
  - Reduction in spleen and liver volumes from baseline
  - Mean change in SRS score
  - Improvement in percentage predicted forced vital capacity (FVC), forced expiratory volume, and total lung capacity
  - Improvement in hematologic and hepatic laboratory values
  - Improvement in linear growth progression (as measured by height Z-scores) (pediatric patients only)

Billing

HCPCS code: J0218, (Injection, olipudase alfa-rpcp, 1 mg)

Required ICD-10-CM Diagnosis Codes

E75.241, E75.244››

Velaglucerase alfa (Vpriv®)

Velaglucerase alfa, which contains the same amino acid sequence as endogenous glucocerebrosidase, catalyzes the hydrolysis of glucocerebroside to glucose and ceramide in the lysosome. In patients with type 1 Gaucher’s disease, glucocerebrosidase deficiency results in accumulation of glucocerebroside in macrophages, thereby causing the associated signs and symptoms. Velaglucerase alfa is used to diminish hepatosplenomegaly and improve anemia, thrombocytopenia, and bone disease.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation that demonstrates the following:

- Must be used for FDA-approved indications and dosages.
- Patient must be four years of age or older
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders
- Patient has a diagnosis of Gaucher disease type 1 diagnosed confirmed by one of the following:
  - Enzyme analysis identifying deficiency of β-glucocerebrosidase activity
  - DNA analysis to identify genetic mutation
- Patient has at least one of the following:
  - Hemoglobin value of greater than or equal to 11.0 g/dL for women and greater than or equal to 12.0 g/dL for men
  - Thrombocytopenia (platelet count less than 100,000/mm3)
  - Splenomegaly, hepatomegaly
  - Disease symptoms such as fatigue, growth retardation, osteopenia/osteoporosis, bony abnormalities and bone pain

Initial authorization is for six months

Continued therapy

- Patient continues to meet initial approval criteria
- Patient has shown positive clinical response as evidenced by at least one of the following changes from baseline:
  - Increase in hemoglobin concentration of at least 1 g/dL
  - Increase in platelet count
  - Decrease in spleen and/or liver volume
  - Reduced bone pain and or/fatigue, bruising and bleeding

Reauthorization is for 12 months

Age Limits

Must be four years of age or older

Billing

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

Suggested ICD-10-CM Diagnosis Codes

E75.22

Prescribing Restrictions

Frequency of billing equals 60 Units/kg every 2 weeks

Vestronidase alfa-vjbk (Mepsevii™)

Vestronidase alfa-vjbk is a recombinant human lysosomal beta glucuronidase. Mucopolysaccharidosis VII (MPS VII or Sly syndrome) is a lysosomal storage disorder caused by deficiency of an enzyme called beta-glucuronidase, which causes an abnormal buildup of toxic materials in the body's cells. Mepsevii is an enzyme replacement therapy that works by replacing the missing enzyme.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Mepsevii will be considered medically necessary if the following criteria are met:

- Must be prescribed for FDA-approved indications and dosing regimens
- Patient must be five months or older
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders
- Patient must have a diagnosis of Mucopolysaccharidosis VII (MPS VII, Sly syndrome) confirmed by one of the following:
  - Enzyme assay of leukocyte or fibroblast with deficiency in beta-glucuronidase
  - Molecular genetic testing with detection of pathogenic mutations in the GUSB gene
- Patient must have at least one of the following documented at baseline:
  - Elevated glycosaminoglycans (uGAG) excretion at a minimum of three-fold over the mean normal for age (at Screening)
  - Bruininks-Oseretsky Test (BOT-2) of Motor Proficiency
  - Shoulder flexion as a measure of limited joint range of motion (ROM)
  - Airway obstruction or pulmonary problems shown by Forced vital capacity (FVC) from pulmonary function testing (PFT)
  - Enlarged liver and/or spleen
  - Limitation of mobility while still ambulatory; confirmed by six-minute walk test (6MWT) or other standard mobility/endurance tests

Initial approval is for six months.

Continued therapy:

- Patient continues to meet the Initial approval criteria
- Patient has shown positive clinical response to therapy from baseline as evidenced by at least one of the following:
  - Reduction in uGAGs excretion.
  - Improvement or stabilization in 6MWT or other standard mobility/endurance test
  - Improvement or stabilization in FVC
  - Reduction in liver and/or spleen volume
  - Improvement or stabilization in joint range of motion
  - Improvement or stabilization in motor skills (BOT-2)

Reauthorization is for 12 months

Age Limits

Must be five months or older

Billing

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

Suggested ICD-10-CM Diagnosis Codes

E76.29

Prescribing Restrictions

Frequency of billing equals 4 mg/kg every 14 days

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 12 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 equals 300 mg/300 units every three months

Maximum billing unit(s) equals 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

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 percent 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 less than or equal to 4,200 mg/week in patients with HIV infection with endogenous serum erythropoietin levels of less than or equal to 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 equals 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 equals 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 equals every 14 days

Maximum billing units equals 6,364 mg equals 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 equals 1 gram/2 units daily for up to 14 days

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

‹‹Esmolol Hydrochloride

Esmolol is a beta$_1$-selective (cardioselective) adrenergic receptor blocking agent with rapid onset, a very short duration of action, and no significant intrinsic sympathomimetic or membrane stabilizing activity at therapeutic dosages.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Billing

HCPCS codes

- J1805 (Injection, esmolol hydrochloride, 10 mg)
- J1806 (Injection, esmolol hydrochloride (WG Critical Care) not therapeutically equivalent to J1805, 10 mg)››

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 (Exondys 51)

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

All FDA-approved indications.

Dosage

All FDA-approved dosages.

TAR/SAR Requirement

An approved *Treatment Authorization Request* (TAR) or California Children's Services (CCS) Program Service Authorization

Request (SAR) is required for reimbursement.

TAR/SAR Criteria

Initial Authorization

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

- Patient must be two years of age or older
- Patient has a documented DMD with dystrophin gene mutation, amenable to exon 51 skipping documented by genetic test(s).
- Care is under the supervision and monitoring of a neurologist, or for CCS patients, a CCS-paneled neurologist or physical medicine and rehabilitation specialist who is fellowship trained in neuromuscular medicine, at a CCS Neuromuscular Medicine Special Care Center (SCC), or at a neurology clinic.
- The following are completed as part of the assessment for antisense oligonucleotide therapy:
  - Forced Vital Capacity (FVC)
  - Brooke score
  - Six minute walk test (6MWT), if ambulatory, and
  - Renal toxicity screening with urinalysis, creatinine/protein ratio or serum cystatin
- The FVC is greater than 30 percent predicted OR the Brooke score is less than or equal to five
- Request for antisense oligonucleotide therapy is for the FDA-approved dosage only
- Only one antisense oligonucleotide treatment shall be authorized at a time
- Patient is on a corticosteroid, or has documented reason not to be on this medication

Initial authorization is for up to 12 months.

Reauthorization

Eteplirsen may be reauthorized for up to one year when the patient has finished the initial course of treatment and all of the following apply:

- Patient has not had significant decline in FVC beyond the pre-treatment disease trajectory while on the antisense oligonucleotide treatment
- Motor function has improved or has not declined beyond pretreatment trajectory, evidenced by improved or maintained score in 6MWT, timed function tests, Performance of Upper Limb (PUL), Brooke score, other standardized assessment of motor function or quantifiable description of improvement by the physician or physical therapist in the medical record
- Patient has not experienced significant adverse effects attributable to eteplirsen

Patients with percent FVC less than or equal to 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.

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

Policy Implementation for CCS Patients

‹‹Submission of authorization requests for eteplirsen is not included in Service Code Groupings (SCGs).››

- 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.
- For patients residing in a dependent county, SARs should be submitted to the CCS dependent county office. The dependent county program office shall pend and submit the SAR and supporting documents to the DHCS ISCD Special Populations Authorization Unit e-mail at CCSOperations@dhcs.ca.gov or via secure RightFax at (916) 440-5768.

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 two years of age or older

Billing

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

Required Codes

ICD-10-CM diagnosis code G71.0

Prescribing Restrictions

Frequency of billing equals 30 mg/kg once weekly

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).

Etranacogene Dezaparvovec-drlb (Hemgenix)

Hemgenix is an adeno-associated virus serotype 5 (AAV5) based gene therapy designed to deliver a copy of a gene encoding the Padua variant of human coagulation Factor IX (hFIX-Padua). Single intravenous infusion of Hemgenix results in cell transduction and increase in circulating Factor IX activity in patients with Hemophilia B.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following:

- Must be used for FDA-approved indications and dosages
- Must be prescribed by or in consultation with a hematologist
- Patient must be male, 18 years of age or older
- Patient has congenital hemophilia B (congenital Factor IX deficiency), classified as severe or moderately severe, FIX deficiency (FIX less than or equal to 2 percent of normal)
- Patient is currently on factor IX prophylaxis, or has current or historical life-threatening hemorrhage, or has repeated, serious spontaneous bleeding episodes
- Patient has had 150 previous exposure days of treatment with factor IX protein
- Patient has had pretreatment hepatic ultrasound and elastography and has no radiological liver abnormalities and/or sustained liver enzymes
- Patient does not have any of the following:
  - History of factor IX inhibitors or Positive factor IX inhibitor test
  - Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin more than 2 times upper limit of normal (ULN)
  - Positive human immunodeficiency virus (HIV) test, not controlled with anti-viral therapy
  - Active infection with hepatitis B or C virus
    - ❖ Patients who have a history of hepatitis B or C exposure must not currently be taking antiviral therapy for hepatitis B or C
  - Previous etranacogene dezaparvovec-drlb treatment
- Outpatient administration is restricted to Hospital Outpatient Services only

Authorization: 3 months (one treatment in a lifetime)

Reauthorization: Never

<u>Important Instructions for Billing</u>

Due to system limitations, providers are to take the following steps when submitting a TAR/SAR and claims for Hemgenix:

<u>TAR/SAR Submission</u>

1. Submit and receive back an approved *Treatment Authorization Request* (TAR) or approved product specific *Service Authorization Request* (SAR).
2. The TAR/SAR is not negotiated.

3. Provider must submit one (1) service line on the TAR/SAR request and enter “4” in the Units box.

Claim Submission

4. Bill using J1411 (injection, etranacogene dezaparvovec-drlb, per therapeutic dose).
5. Completion of claim forms:
   - This billing methodology is restricted to hospital outpatient services. Note that pharmacies and clinics cannot bill using this methodology.
   - Outpatient claims may be billed electronically or by paper claim using 837I (Institutional) or UB-04 Medi-Cal claim forms with the following conditions:
     - ❖ On the 837I or UB-04 claim form, provider must submit four (4) claim lines to represent one (1) service.
       - Each claim line to represent one unit.

Claims submitted with one or two claim lines will be denied.

- ❖ Provider must submit an invoice for reimbursement.
- ❖ This process will ensure that the total reimbursement paid for the four (4) claim lines is no more than the paid price on the provider submitted invoice.
- ❖ Hemgenix must be billed on its own with no other drug or biological.

6. Providers are advised to take the following steps to ensure that Hemgenix claims are identified and processed expeditiously:
   - Paper claims may be identified by notation of “Hemgenix” on the “Remarks” section of the UB-04 claim form (Field #80) and submitted to:

     Attention: Claims Manager
     Medi-Cal Fiscal Intermediary
     P.O. Box 526006
     Sacramento, CA 95852-6006
   - Electronic claims may be identified by notation of “Hemgenix” on the cover sheet, addressed to Attention: Claims Manager and submitted with the 837I claim form.
7. Providers to note that except for the first claim line, payment for any additional line will be delayed for two to three additional weeks due to systems constraints.
8. Payment for Hemgenix shall be once in a lifetime reimbursement under J1411 or any other code (HCPCS, CPT® or by NDC).
9. For instructions regarding physical claim form completion, refer to the Forms page on the Medi-Cal Providers website and forms section *UB-04 Completion: Outpatient Services* for completion of 837I and *UB-04* claim forms.

Age Limits

Must be 18 years of age or older

Billing

HCPCS code J1411, (Injection, etranacogene dezaparvovec-drlb, per therapeutic dose)

Required ICD-10 Diagnosis Codes

D67

Prescribing Restriction(s)

Frequency of billing is one treatment in a lifetime.

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 six 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

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

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 equals 1,000 mg/100 units for one dose. May repeat dose if iron deficiency anemia reoccurs.

Maximum billing unit(s) equals 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 equals Initial 510 mg/510 units dose followed by a second 510 mg/510 units dose three to eight days later.

Maximum billing unit(s) equals 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-aafi (Nvestym™), Filgrastim-sndz (Zarxio®)

See *Chemotherapy: Drugs E-O Policy* in the appropriate Part 2 manual for policy pertaining to filgrastim, filgrastim-aafi and filgrastim-sndz and the corresponding procedure codes.

Fomepizole

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

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 equal to or greater than 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

‹‹Furosemide (FUROSCIX®)

Furosemide primarily inhibits the reabsorption of sodium and chloride in the proximal and distal tubules and in the loop of Henle. The high degree of diuresis is largely due to the unique site of action. The action on the distal tubule is independent of any inhibitory effect on carbonic anhydrase and aldosterone.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following:

- Must be used for FDA-approved indications and dosage
- Patient has a diagnosis of NYHA Class II or Class III chronic heart failure
- Patient must be 18 years of age or older
- Patient has an active prescription for an oral diuretic, equivalent to a daily total furosemide dose of 40 to 160 mg
- Provider attests that the patient is showing signs of volume expansion due to chronic heart failure››

- ‹‹Provider must show justification for failure to use furosemide intravenous injection
- Patient is stable and suitable for at-home treatment with parenteral diuresis as evidenced by all of the following:
  - Oxygen saturation is at least 90 percent on exertion
  - Respiratory rate is less than 24 breaths per minute
  - Resting heart rate is less than 100 beats per minute
  - Systolic blood pressure is more than 100 mmHg

Authorization is for 12 months

Age Limits

Must be 18 years of age or older

Billing

HCPCS code J1941 (Injection, furosemide (Furoscix), 20 mg)

Prescribing Restriction(s)

Maximum billing unit(s) equal 80 mg/4 units››

Ganciclovir Injection (GANZYK-RTU)

Ganciclovir is phosphorylated by viral and cellular kinases into ganciclovir triphosphate which competitively inhibits the binding of deoxyguanosine triphosphate to DNA polymerase resulting in inhibition of viral DNA synthesis.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

TAR Criteria

Ganciclovir 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 and older.
- Ganciclovir is being used under one of the following conditions:
  - Patient is immunocompromised or has acquired immunodeficiency syndrome (AIDS) and ganciclovir is being used for the treatment of cytomegalovirus (CMV) retinitis.
  - Patient is a transplant recipient at risk for CMV and ganciclovir is being used for the prevention of CMV disease.
- Patient has no history of hypersensitivity to acyclovir or ganciclovir.
- Oral antiviral products (for example, valganciclovir, ganciclovir, etc.) are not clinically appropriate.

Patient must meet A or B below:

A. Treatment of CMV Retinitis

- Patient is immunocompromised or has AIDS and has a diagnosis of CMV retinitis by ophthalmologic examination

B. Prevention of CMV Disease in Transplant Recipients

- Patient meets one of the following criteria:
  - Patient is an organ transplant recipient and is at risk of CMV infection (CMV seropositive or a seronegative recipient of an organ from a CMV seropositive donor).
  - Patient is a bone marrow recipient with asymptomatic CMV infection (CMV positive culture of urine, throat or blood)
  - Patient is an allogeneic bone marrow transplant recipient at risk for CMV disease (Patients with histologic, immunologic or virologic evidence of CMV infection in the lung post-transplant)

Authorization is for six months.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code J1574 (injection, ganciclovir sodium [exela] not therapeutically equivalent to J1570, 500 mg).

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)

Givosiran (Givlaari®)

Givosiran causes degradation of aminolevulinate synthase 1 (ALAS1) messenger RNA (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 and porphobilinogen, factors associated with attacks and other disease manifestations of acute hepatic porphyria.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following:

- Must be for FDA-approved indications and dosages
- Patient must be 18 years of age or older
- Must be prescribed by or in consultation with a hematologist, neurologist, gastroenterologist, or other provider with expertise in Acute Hepatic Porphyria (AHP).
- Patient has a diagnosis of AHP (Acute Intermittent Porphyria [AIP), Hereditary Corproporhyria [HCP], Variegate Porphyria [VP], aminolevulinic acid [ALA] dehydratase deficient porphyria [ADP]).
- Genetic testing results was according to 1 or 2 below:
    1. Shows evidence of mutation in a porphyria-related gene, defined as ANY of the following:
        - ❖ AIP: mutation in the hydroxymethylbilane synthase gene (HMBS; also referred to as the orphobilinogen deaminase [PBGD] gene)
        - ❖ HCP: mutation in the coproporphyrinogen oxidase (CPOX) gene
        - ❖ VP: mutation in the protoporphyrinogen oxidase (PPOX) gene
        - ❖ ADP: mutation in the aminolevulinic acid dehydratase (ALAD) homozygous or compound heterozygous genes; OR
    2. Does not identify a mutation in a porphyria-related gene (less than 5 percent of cases), but patient has both clinical features and diagnostic biochemical criteria consistent with AHP.
- Patient has at least one documented urinary or plasma porphobilinogen (PBG) or ALA values within the 12 months
- Patient has active disease, with at least two documented porphyria attacks within prior 6 months requiring hospitalization, urgent healthcare visit OR
    - Patient requires hemin prophylaxis to prevent this frequency of attacks

- Patient does not have any of the following:
  - A clinically significant abnormal laboratory results, including renal and hepatic function tests.
  - Anticipated liver transplantation

Initial authorization is for 12 months

Continued therapy:

- Patient continues to meet the initial approval criteria
- Patient has shown clinical benefit as evidenced by at least one of the following:
  - Reduction in the rate of porphyria attacks requiring hospitalizations, urgent healthcare visit, or intravenous hemin administration at home
  - Reduction in ALA or PBG levels from baseline
  - Improvement in signs and symptoms of AHPs (for example, neurological, peripheral neuropathy, abdominal pain, muscle aches, weakness, etc.)
  - 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.)

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 equals 2.5 mg/kg every month

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

Glucagon

Glucagon increases blood glucose concentration by activating hepatic glucagon receptors, thereby stimulating glycogen breakdown and release of glucose from the liver. Hepatic stores of glycogen are necessary for glucagon to produce an antihypoglycemic effect. Extrahepatic effects of glucagon include relaxation of the smooth muscle of the stomach, duodenum, small bowel, and colon.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Billing

HCPCS codes:

J1610 (injection, glucagon hydrochloride, per 1 mg).

J1611 (injection, glucagon hydrochloride [fresenius kabi], not therapeutically equivalent to J1610, per 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 California Children's Services (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. Patient must be 2 years of age or older
2. Patient has documented Duchenne muscular dystrophy (DMD) with dystrophin gene mutation, amenable to exon 53 skipping documented by genetic test(s)
3. Care is under the supervision and monitoring of a neurologist; or for CCS patients, a CCS-paneled neurologist or physical medicine and rehabilitation specialist who is fellowship-trained in neuromuscular medicine, at a CCS Neuromuscular Medicine Special Care Center (SCC) or a neurology clinic
4. The following are completed as part of the assessment for antisense oligonucleotide therapy:
    a) Forced vital capacity (FVC)
    b) Brooke score
    c) 6-minute walk test (6MWT), if ambulatory, and

d) Renal toxicity screening with urinalysis, creatinine/protein ratio or serum cystatin C

5. The FVC is greater than 30% predicted OR the Brooke score is less than or equal to 5
6. Request for antisense oligonucleotide therapy is for the FDA-approved dosage only
7. Only one antisense oligonucleotide treatment shall be authorized at a time
8. Patient is on a corticosteroid or has documented reason not to be on this medication

Initial authorization is for up to 12 months

B. Reauthorization

Golodirsen shall be reauthorized for up to 12 months when the patient has finished the initial course of treatment and all of the following apply:

1. Patient has not had significant decline in FVC beyond the pre-treatment disease trajectory while on the antisense oligonucleotide treatment.
2. Motor function has improved, or has not declined beyond pre-treatment trajectory, evidenced by improved or maintained score in 6MWT, time function tests, Performance of Upper Limb (PUL), Brooke score, 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 FVC less than or equal to 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 patients 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 patient'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)

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 the CCS dependent county office. The dependent county program office shall pend and submit the SAR and supporting documents to the 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 two years of age or older

Billing

HCPCS code J1429 (injection, golodirsen, 10 mg)

Required 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 (Sustol®)

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. Animal studies demonstrate that, in binding to 5-HT3 receptors, granisetron blocks serotonin stimulation and subsequent vomiting after emetogenic stimuli such as cisplatin. In the ferret animal model, a single granisetron injection prevented vomiting due to high-dose cisplatin or arrested vomiting within 5 to 30 seconds.

Indications

All FDA-approved indications

Dosage

All FDA-approved dosages

TAR Requirement

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

TAR Criteria

Must submit clinical documentation to substantiate the following:

- Must be used for FDA-approved indications and dosages
- Patient must be 18 years of age or older
- Patient is scheduled to undergo cancer chemotherapy
- Sustol is being used in combination with other antiemetics (for example aprepitant or fosaprepitant, and dexamethasone or olanzapine, etc) for the prevention of acute and delayed nausea and vomiting associated with one of the following:
  - Initial and repeat courses of moderately emetogenic chemotherapy (MEC)
  - Anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.

Authorization is for six months

Age Limits

Must be 18 years of age or older

Billing

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

Suggested ICD-10 Diagnosis Codes

ICD-10-CM diagnosis codes: R11.0, R11.10, R11.11, R11.12, R11.2, and Z51.11

Prescribing Restriction(s)

Frequency of billing equals 10 mg/100 units once every seven days

Maximum billing unit(s) is 10 mg/100 units

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.

Heparin

Heparin interacts with the naturally occurring plasma protein. Antithrombin III, to induce a conformation change, which markedly enhances the serine protease activity of Antithrombin III, thereby inhibition the activated coagulation factors involved in the clotting sequence, particularly Xa and IIA. Small amount of the Factor XA and larger amounts inhibit thrombin (Factor IIA). Heparin also prevents the formation of stable fibrin clot by inhibiting the activation to the fibrin stabilizing factor. Heparin does not have fibrinol activity, therefore, it will not lyse existing clots.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

Billing

HCPCS codes:

J1643 (injection, heparin sodium [pfizer], not therapeutically equivalent to J1644, per 1000 units).

J1644 (injection, heparin sodium, per 1000 units).

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

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.