Injections: Drugs E 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:

- *Immunizations*
- *Injections: Drugs A Policy*
- *Injections: Drugs B Policy*
- *Injections: Drugs C Policy*
- *Injections: Drugs D Policy*
- *Injections: Drugs F Policy*
- *Injections: Drugs G Policy*
- *Injections: Drugs H Policy*
- *Injections: Drugs I Policy*
- *Injections: Drugs J-L Policy*
- *Injections: Drugs M Policy*
- *Injections: Drugs N-O Policy*
- *Injections: Drugs P-Q Policy*
- *Injections: Drugs R Policy*
- *Injections: Drugs S Policy*
- *Injections: Drugs T Policy*
- *Injections: Drugs U-Z Policy*
- *Injections: Hydration*

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 Limit

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 equals 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) equals 1,200 mg equals 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 Limit

Must be18 years of age 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 and Hyaluronidase-qvfc (VYVGART Hytrulo™)

VYVGART 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).

VYVGART Hytrulo is a coformulation of efgartigimod alfa and hyaluronidase. Efgartigimod alfa is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan. This effect is transient and permeability of the subcutaneous tissue is restored within 24 to 48 hours.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

TAR Criteria

‹‹The TAR must include clinical documentation that demonstrates all of the following:

- Must be used for FDA-approved indications and dosages.
- Must be prescribed by or in consultation with a neurologist.
- Patient is at least 18 years of age.
- 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 approval is for six months.

Continued therapy criteria:

- 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 six months.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS codes:

J9332 (injection, efgartigimod alfa-fcab, 2mg).

J9334 (injection, efgartigimod alfa, 2 mg and hyaluronidase-qvfc)

Required ICD-10 Diagnosis Codes

G70.00, G70.01

Prescribing Restriction(s)

VYVGART

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

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

VYVGART Hytrulo

Frequency of billing equals 1,008 mg (504 units)/11,200 units (1,008 mg efgartigimod alfa and 11,200 units hyaluronidase) once a week for four weeks.

Maximum billing unit(s) equals 1008 mg (504 units)/11200 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 five out of eight 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 (i.e., 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 one 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 (less than 50 percent 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 equal to or greater than 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 Limit

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 (equal for greater than five 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)
- ‹‹Cipaglucosidase alfa-atga (POMBILITI)››
- Elosulfase Alfa (Vimizim®)
- Galsulfase (Naglazyme®)
- Idursulfase (Elaprase®
- Imiglucerase (Cerezyme)
- Laronidase (Aldurazyme®)
- ‹‹Miglustat (OPFOLDA)››
- Olipudase Alfa-rpcp (Xenpozyme)
- Pegunigalsidase alfa-iwxj (Elfabrio®)
- Velaglucerase Alfa (Vpriv)
- Velmanase alfa-tycv (Lamzede®)
- 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 Limit

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).

HCPCS code 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 Limit

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 Limit

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.

‹‹Cipaglucosidase alfa-atga (POMBILITI)

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 lysosomal acid alpha-glucosidase (GAA) that degrades glycogen to glucose in the lysosome. GAA deficiency results in intra-lysosomal accumulation of glycogen in various tissues.

Cipaglucosidase alfa-atga provides an exogenous source of GAA. The bis-M6P on cipaglucosidase alfa-atga 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 and N-glycans trimming which are both required to yield the most mature and active form of GAA. Cipaglucosidase alfa-atga then exerts enzymatic activity in cleaving glycogen.

Miglustat binds with, stabilizes, and reduces inactivation of cipaglucosidase alfa-atga in the blood after infusion.››

‹‹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.
- Must be 18 years of age or older and weigh at least 40 kg.
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders.
- 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 documented baseline results of Forced Vital Capacity (FVC) and/or six Minute Walk Test (6MWT) or motor function.
- Patient has not shown a functional or measurable improvement such as change in FVC or 6MWT after receiving Avalglucosidase Alfa-ngpt (Nexviazyme™ or Alglucosidase alfa (Lumizyme®) for at least one year.
- POMBILITI will be administered in combination with Opfolda

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.

Reauthorization is for 12 months.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code: J1203, Injection, cipaglucosidase alfa-atga, 5 mg

Suggested ICD-10-CM Diagnosis Codes

E74.02

Prescribing Restrictions

Frequency of billing equals 20 mg/kg every other week››

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 Limit

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 Limit

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 Limit

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 Limit

Must be two years of age or older.

Billing

HCPCS code J1786 (injection, imiglucerase, per 10 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.

<u>Continuation of therapy</u>

- 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 Limit

Must be six months of age 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.

‹‹Miglustat (OPFOLDA)

Miglustat binds with, stabilizes, and reduces inactivation of cipaglucosidase alfa-atga in the blood after infusion. The bound miglustat is dissociated from cipaglucosidase alfa-atga after it is internalized and transported into lysosomes. Miglustat alone has no pharmacological 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:

- Must be used for FDA-approved indications and dosages.
- Must be 18 years of age or older and weigh at least 40 kg.
- Must be prescribed by or in consultation with a geneticist or other physician with specialty in treating metabolic disorders.
- 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 documented baseline results of Forced Vital Capacity (FVC) and/or six Minute Walk Test (6MWT) or motor function.
- Patient has not shown a functional or measurable improvement such as change in FVC or 6MWT after receiving Avalglucosidase Alfa-ngpt (Nexviazyme™) or Alglucosidase alfa (Lumizyme®) at the recommended dose and regimen for at least one year.
- Opfolda will be administered in combination with Pombiliti.
- Patient is not a pregnant female.

Initial authorization is for 12 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.››

‹‹Reauthorization is for 12 months.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code J1202, Miglustat, oral, 65 mg

Required ICD-10-CM Diagnosis Codes

E74.02

Prescribing Restrictions
Frequency of billing equals 260 mg/ four units every other week

Maximum billing units equals 260 mg/ four units

Billing Instructions:

Provider may bill G0138 for reimbursement of the administration fee.››

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 one 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 two 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 six multiples of normal (MN) measured by MRI
  - Splenomegaly related score (SRS) are greater than or equal to five
    - 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

Pegunigalsidase alfa-iwxj (Elfabrio®)

Fabry disease is caused by deficiency of the lysosomal enzyme alpha-galactosidase A. Elfabrio provides an exogenous source of alpha-galactosidase A. Elfabrio is internalized and transported into lysosomes where it is thought to exert enzymatic activity and reduce accumulated globotriaosylceramide (Gb3).

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

TAR Criteria

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

- 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 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 three percent) in males
  - Presence of Globotriaosylceramide (Gb3) and globotriaosylsphingosine (lysoGb3) in the plasma and urine
- Documentation of one or more 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.
- Elfabrio will not be used concurrently with another enzyme replacement therapy or Galafold (migalastat).

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 renal function, pain reduction from baseline

Reauthorization is for 12 months.

Age Limit

Must be 18 years of age or older.

Billing

HCPCS code J2508, (injection, pegunigalsidase alfa-iwxj, 1 mg).

Required ICD-10-CM Diagnosis Codes

E75.21

Prescribing Restrictions

Frequency of billing equals 1 mg/kg every two weeks.

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 Limit

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 two weeks.

Velmanase alfa-tycy (LAMZEDE®)

Alpha-mannosidosis is a lysosomal storage disease that results from reduced activity of the enzyme alpha-mannosidase, caused by gene variants in Mannosidase Alpha Class 2B Member 1. Alphamannosidase catalyzes the degradation of accumulated mannose-containing oligosaccharides. The deficiency of alpha-mannosidase causes an intra-lysosomal accumulation of mannose-rich oligosaccharides in various tissues. Velmanase alfa-tycv provides an exogenous source of alphamannosidase. Velmanase alfa-tycv is internalized via binding to the mannose-6-phosphate receptor on the cell surface and transported into lysosomes where it is thought to exert enzyme activity.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

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

TAR Criteria

The TAR must include documentation that demonstrates the following:

- Must be used for FDA-approved indications and dosages.
- Patient has a diagnosis of alpha-mannosidosis, based on:
  - Deficient levels or activity of the enzyme alpha-mannosidase measured in blood leukocytes or fibroblasts or
  - Genetic testing revealing a variant in the MAN2B1 gene.
- Patient presents with non-central nervous system manifestations of alpha-mannosidosis.
- Patient is not pregnant. Advise females of reproductive potential to use effective contraception during treatment and for 14 days after the last dose if Lamzede is discontinued.

Initial authorization is for 12 months.

Continued therapy

- Patient continued to meet initial approval criteria.
- Positive clinical response as evidenced by disease improvement or stabilization compared to baseline.

Reauthorization is for 12 months.

Age Limit

Must be 64 years of age or younger.

Billing

HCPCS code J0217 (injection, velmanase alfa-tycv, 1 mg).

Required ICD-10-CM Diagnosis Codes

E77.1

Prescribing Restriction(s)

Frequency of billing equals 1 mg/kg weekly.

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 Limit

Must be five months of age 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 four 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 Limit

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 Limit

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 Limit

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 two percent of normal).
- ‹‹Patient has severe bleeding phenotype defined by:
  - FIX Therapy
    - ❖ Currently on prophylactic FIX replacement therapy for a history of bleeding or
    - ❖ Currently receiving on-demand therapy with a current or past history of frequent bleeding defined as four or more bleeding episodes in the last 12 months or chronic hemophilic arthropathy (pain, joint destruction, and loss of range of motion) in one or more joints, and
  - Has had over 150 exposure days of treatment with FIX 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 and Hemophiliac Treatment Centers (HTCs) only.››

Authorization: three months (one treatment in a lifetime)

Reauthorization: Never

Important Instructions for Billing

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

TAR/SAR Submission

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 Limit

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 three 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 eight 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 three 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.

Continued Therapy

- 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 four weeks).

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.