Original Effective Date: 12/01/2014
Current Effective Date: 10/09/2024
Last P&T Approval/Version: 07/31/2024
Next Review Due By: 07/2025
Policy Number: C6633-A

Cerdelga (eliglustat)

PRODUCTS AFFECTED

Cerdelga (eliglustat)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Type 1 Gaucher Disease

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. TYPE 1 GAUCHER DISEASE (GD):
1. Documented diagnosis of Type 1 Gaucher disease (GD)
AND

2. Documentation diagnosis was confirmed by Glucocerebrosidase activity in the white blood cells or skin fibroblasts less than or equal to 30% of normal activity OR genotype testing indicating a mutation of two alleles of the glucocerebrosidase genome [DOCUMENTATION REQUIRED].
   AND
3. Documentation of member experiencing any of the following signs/symptoms indicating severe manifestations where enzyme replacement therapy (ERT) or alternative substrate reduction therapy (SRT) is recommended: splenomegaly, anemia, thrombocytopenia, diffuse bone pain, vertebral compression fractures, fragility fractures, interstitial lung disease, elevated basal metabolic rate, insulin resistance, lipid abnormalities, hepatic or splenic infarcts, hepatitis, portal hypertension, hepatomegaly, avascular necrosis, or lytic disease
   AND
4. Documentation of rationale as to why enzyme replacement therapy [i.e., imiglucerase (Cerezyme), velaglucerase (Vpriv), taliglucerase (Elelyso)] is NOT a therapeutic option, such as but not limited to the following: Refractory or intolerant to enzyme replacement therapy, Allergic to components of, or hypersensitivity to enzyme replacement therapy, or Poor venous access
   AND
5. Documentation of member's therapeutic goals based on their individual baseline symptoms (e.g., bone pain, fatigue, dyspnea, angina, abdominal discomfort), overall health, and quality of life
   AND
6. Documentation that an FDA-cleared genotyping test has determined that member is a CYP2D6 Extensive metabolizer (EM), Intermediate metabolizer (IM), or Poor metabolizer (PM) [DOCUMENTATION REQUIRED]
   NOTE: A CYP2D6 genotype testing is available through a Sanofi Genzyme-funded genotyping program with LabCorp at one of 1700 LabCorp draw stations
   AND
7. Provider attestation that Cerdelga (eliglustat) will be monotherapy and NOT used concomitantly with other therapies for Type 1 GD: Zavesca (miglustat), Cerezyme (imiglucerase), Elelyso (taliglucerase alfa), or VPRIV (velaglucerase alfa)
   AND
8. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Cerdelga (eliglustat) include: avoid use in patients with pre-existing cardiac disease (congestive heart failure, recent acute myocardial infarction, bradycardia, heart block, ventricular arrhythmia), avoid use in patients with long QT syndrome, avoid use in combination with Class IA (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, contraindication in the following patients based on CYP2D6 metabolizer status due to the risk of cardiac arrhythmias from prolongation of the PR, QTc, and/or QRS cardiac intervals:

   Extensive metabolizers (EMs):
   - Moderate or severe hepatic impairment
   - Mild hepatic impairment taking a strong or moderate CYP2D6 inhibitor
   - Taking a strong or moderate CYP2D6 inhibitor concomitantly with a strong or moderate CYP3A inhibitor
   - Avoid in patients with end stage renal disease (ESRD) (estimated CrCl less than 15mL/min or requiring dialysis)

   Intermediate metabolizers (IMs):
   - Taking a strong or moderate CYP2D6 inhibitor concomitantly with a strong or moderate CYP3A inhibitor
   - Taking a strong CYP3A inhibitor
   - Any degree of hepatic impairment
   - Avoid in patients with any degree of renal impairment

   Poor metabolizers (PMs):
   - Any degree of hepatic impairment

- Taking a strong CYP3A inhibitor
- Avoid in patients with any degree of renal impairment]

CONTINUATION OF THERAPY:

A. TYPE 1 GAUCHER DISEASE (GD):

1. Documentation of improvement in, or stabilization from, baseline based on member's therapeutic goals which may include any of the following: spleen volume, hemoglobin level, liver volume, platelet count (sufficient to decrease the risk of bleeding), growth, bone pain or crisis
   AND
2. Prescriber attests a recent review of member's current medication has been completed and there is no concomitant use of CYP2D6 and CYP3A inhibitors (a contraindication) per metabolizer status
   AND
3. Provider attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with, a board-certified geneticist, metabolic specialist, hematologist, or physician experienced in the management of Gaucher Disease. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Extensive (EMs) and Intermediate metabolizers (IMs): 84mg twice daily
Poor metabolizers (PMs): 84mg once daily

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

Agents for Gaucher Disease

FDA-APPROVED USES:

Indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are cytochrome P450 (CYP- 450) 2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test.
Limitations of use: *Individuals who are CYP2D6 ultra-rapid metabolizers may not achieve adequate concentrations of eliglustat to achieve a therapeutic effect. A specific dosage cannot be recommended for those patients whose CYP2D6 genotype cannot be determined (indeterminate metabolizers).*

COMPENDIAL APPROVED OFF-LABELED USES:

None

APPENDIX

APPENDIX:

Cytochrome P450 2D6 (CYP2D6) inhibitors (list not all-inclusive)
Strong inhibitors: Bupropion, Dacomitinib, Fluoxetine, Paroxetine, Quinidine, Tipranavir

Moderate inhibitors: Abiraterone, Asunaprevir, Cinacalcet, Darifenacin, Darunavir, Duloxetine, Lorcaserin, Mirabegron, Rolapitant, Terbinafine (systemic), Thioridazine

Cytochrome P450 3A (including 3A4) inhibitors (list not all-inclusive)
Strong inhibitors: Atazanavir, Clarithromycin, Cobicistat and cobicistat-containing coformulations, Darunavir, Idelalisib, Indinavir, Itraconazole, Ketoconazole, Lopinavir, Mifepristone, Nefazodone, Nelfinavir, Ombitasvir-paritaprevir-ritonavir, Ombitasvir-paritaprevir-ritonavir plus dasabuvir, Posaconazole, Ritonavir and ritonavir-containing coformulations, Saquinavir, Telithromycin, Voriconazole

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Gaucher Disease (GD) is a rare, autosomal recessive, lysosomal storage disorder caused by mutations in the glucocerebrosidase gene, resulting in the accumulation of glucosylceramide in macrophage cells. GD is characterized by hepatosplenomegaly, thrombocytopenia, and anemia, and is classified into 3 major types and 2 subtypes. There are 3 subtypes based on characteristic patterns of clinical signs and age of onset, GD is subdivided into three main disease variants: type 1 (non- neuronopathic), type 2 (acute neuronopathic), and type 3 (subacute neuronopathic).

- Type 1 (nonneuropathic form): bone disease and lack of primary central nervous system involvement
- Type 2 (acute neuronopathic form): severe neurologic impairment without bone involvement
- Type 3 (chronic or subacute neuronopathic form): neurologic impairment and bone disease subtype fetal or perinatal-lethal form: death in utero or shortly afterbirth

Type I Gaucher Disease (GD1) is an inherited disease caused by a functional deficiency of glucocerebrosidase, the enzyme that mediates degradation of the glycosphingolipid glucosylceramide. The failure to degrade glucosylceramide results in the lysosomal storage of this lipid material within tissue macrophages leading to widespread pathology. Macrophages containing stored glucosylceramide are typically found in the liver, spleen, and bone marrow and occasionally in the lung, kidney, and intestine. Secondary hematologic consequences include severe anemia and thrombocytopenia in addition to the characteristic progressive hepatosplenomegaly. Skeletal complications include osteonecrosis and osteopenia with secondary pathological features. Common manifestations of GD include anemia, hepatomegaly, splenomegaly, thrombocytopenia, and skeletal abnormalities (bone pain, bone crisis, growth retardation, osteopenia).

The decision to treat with enzyme-replacement therapy (ERT) or substrate-reduction therapy (SRT) in nonneuronopathic (type 1) GD is based upon disease severity, as determined by the initial assessment, or significant disease progression, as established through regular follow-up. Goals of treatment are elimination or improvement of symptoms, prevention of irreversible complications, and improvement in overall health and quality of life. Additional goal in children is optimization of growth. ERT (imiglucerase, velaglucerase, or taliglucerase) or SRT are preferred treatments for members with clinically significant manifestations of non- neuronopathic GD (Type 1). ERT is the standard of care and is recommended for symptomatic pediatric members and for members with severe manifestations of nonneuronopathic GD1. Available therapies for GD1 include intravenous ERT (Cerezyme, VPRIV, and Elelyso) and oral substrate reduction therapy (Cerdelga, Zavesca).

- Type 1 Gaucher disease is caused by a functional deficiency of glucocerebrosidase, the enzyme that mediates the degradation of the glycosphingolipid glucosylceramide.
- Eliglustat competitively and reversibly inhibits the enzyme needed to produce glycosphingolipids and decreases the rate of glycosphingolipid glucosylceramide formation. Glucosylceramide accumulates in

type1 Gaucher disease, causing complications specific to this disease.

- The goal of treatment with eliglustat is to reduce the rate of glycosphingolipid glucosylceramide biosynthesis so that the amount of glycosphingolipid substrate is reduced to a level which allows the residual activity of the deficient glucocerebrosidase enzyme to be more effective (substrate reduction therapy).

Cerdelga (eliglustat) may be authorized for second-line treatment in Type I GD for adult members with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option when appropriate criteria are met.

- Eliglustat should be considered an alternative to enzyme replacement therapy with beta-glucocerebrosidase (i.e., alglucerase or imiglucerase) in members with confirmed non- neuronopathic Gaucher's disease (GD).

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Cerdelga (eliglustat) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy.

Contraindications to Cerdelga (eliglustat) include: Use in extensive metabolizers (EMs) with moderate or severe hepatic impairment; use in intermediate metabolizers (IMs) or poor metabolizers (PMs) with any degree of hepatic impairment; concomitant use of a moderate or strong CYP2D6 inhibitor with a moderate or strong CYP3A inhibitor in EMs or IMs; concomitant use of a strong CYP3A inhibitor in PMs or IMs; concomitant use of a moderate or strong CYP2D6 inhibitor in EMs with mild hepatic impairment; avoid use in pre-existing cardiac disease (congestive heart failure, recent acute myocardial infarction, bradycardia, heart block, ventricular arrhythmia); Long QT syndrome; Concomitant use with Class IA (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications (has not been studied); Renal impairment: Avoid use in IMs and PMs with any degree of renal impairment and in Ems with ESRD.

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:

Cerdelga CAPS 84MG

REFERENCES

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11. Wang RY, Bodamer OA, Watson MS, et al. American College of Medical Genetics: Lysosomal Storage Diseases: Diagnostic Confirmation and Management of Presymptomatic Individuals. Genetics in Medicine. 2011; 13(5):464-466.
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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information References	Q3 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Quantity FDA-Approved Uses References	Q3 2023
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements Background Contraindications/Exclusions/Discontinuation References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file