Medical Drug Clinical Criteria

Subject:	Enzyme Replacement Therapy for Gaucher Disease		
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Overview

This document addresses the use of Cerezyme (imiglucerase), Elelyso (taliglucerase) and Vpriv (velaglucerase), enzyme replacement therapies approved by the Food and Drug Administration (FDA) for the treatment of adults and children with a confirmed diagnosis of type 1 Gaucher disease.

Gaucher disease is a rare autosomal recessive disease characterized by a deficiency of glucocerebrosidase, an enzyme vital to the breakdown of glucosylceramide. Impairment of glucocerebrosidase leads to the collection of glucosylceramide in cells in the spleen, liver, bones and bone marrow. The primary clinical manifestations of Gaucher disease include splenomegaly, hepatomegaly, anemia, thrombocytopenia and skeletal complications. Symptomatic skeletal disease includes avascular necrosis, Erlenmeyer flask deformity, lytic disease, marrow infiltration, osteopenia, osteosclerosis, pathological fracture and joint deterioration. In some forms of Gaucher disease, the collection of glucosylceramide is seen in the brain, resulting in neurologic impairment and dysfunction. Manifestations of neurologic disease include seizures, eye movement and vision problems, poor coordination and progressive brain damage.

Diagnosis of Gaucher disease involves clinical examination, radiological imaging and laboratory testing. Glucocerebrosidase enzyme activity measurement and genotype testing of the glucocerebrosidase genome are important to avoid confusion with other diseases, including other lipidoses. Assessment and confirmation of neurologic disease must include a thorough neurological examination that includes eye movement examination, measurement of peripheral hearing, brain imaging, electroencephalography and age-appropriate neuropsychometry.

There are three presentations of Gaucher disease. Type 1 is the most common form of Gaucher disease, responsible for approximately 90% of all cases. The age of onset for type 1 Gaucher disease is highly variable with symptom presentation occurring anywhere from childhood to late adulthood. Alternatively, some individuals with this genotype of Gaucher disease never have any symptoms. Commonly seen symptoms of type 1 Gaucher disease include fatigue, cachexia, growth delay in childhood and easy bruising or bleeding. Individuals exhibit the visceral, hematologic and bone manifestations of disease which progress in severity over time. There is no neurologic involvement with type 1 Gaucher disease.

Type 2, also referred to as neuropathic Gaucher disease, is the rarest form of this disease. Type 2 Gaucher disease is characterized by early age of onset with serious, rapidly progressive neurologic deterioration and less severe visceral impairment. Widespread neurological dysfunction leading to severe seizures, rigidity and other motor dysfunction is common.

Type 3 Gaucher disease is a less severe neuropathic form of disease compared to type 2. The age of onset may occur anywhere from early childhood to late adulthood and the course of the disease is much more variable than with the other types. Type 3 Gaucher disease typically has a more aggressive presentation of visceral, hematologic and bone involvement than type 1 disease. Type 3 Gaucher disease does include neurologic dysfunction, with poor coordination, paralysis of the eye muscles, and dementia; however, the severity of these conditions is much less than with type 2 Gaucher disease.

Clinical studies have demonstrated the systemic manifestations of type 1 Gaucher disease, including visceral, hematologic and bone symptoms, respond well to enzyme replacement therapy (ERT) with glucocerebrosidase analogs. Similar benefits have been shown for systemic manifestations of type 3 Gaucher disease. Unfortunately, the glucocerebrosidase analogs do not pass through the blood-brain barrier and have minimal to no impact on the neurologic symptoms seen in type 2 and type 3 Gaucher disease.

Cerezyme, Elelyso and Vpriv are glucocerebrosidase analogs approved by the FDA for long-term treatment of type 1 Gaucher disease in adults and children who are exhibiting systemic disease manifestations. Small case series have been published that support the use of ERT for controlling visceral, bone and hematologic symptoms in type 3 Gaucher disease. Kaplan and colleagues (2013) published updated recommendations for the management of children with Gaucher disease. Enzyme replacement therapy was recommended for all symptomatic children with type 1 and 3 Gaucher disease to prevent debilitating and often irreversible disease progression.

The clinical trial programs for both Vpriv and Elelyso included participants who switched from Cerezyme to Vpriv or Elelyso. The FDA determined there was sufficient evidence of safety and efficacy in this situation and that Vpriv and Elelyso are alternatives for individuals currently receiving treatment for Gaucher disease with Cerezyme. The dosage and administration section of product labeling includes dosing recommendations for switching from Cerezyme to Vpriv or Elelyso.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Enzyme Replacement Therapy for Gaucher Disease [Cerezyme (imiglucerase), Elelyso (taliglucerase), Vpriv (velaglucerase)]

Initial requests for enzyme replacement therapy for Gaucher disease [Cerezyme (imiglucerase), Elelyso (taliglucerase) and Vpriv (velaglucerase)] may be approved if the following criteria are met:

I. Individual is 18 years of age or older with a diagnosis of t**ype 1** Gaucher disease and the following criteria are met:
   A. Documentation is provided that Type 1 Gaucher disease is confirmed by either (Weinreb, 2004; Wang, 2011):
      1. Deficiency in glucocerebrosidase enzyme activity as measured in the white blood cells or skin fibroblasts; **OR**
      2. Genotype testing indicates mutation of two alleles of the glucocerebrosidase genome; **AND**
   B. Documentation is provided that individual has clinically significant manifestations of Gaucher disease including (Andersson, 2005; Weinreb, 2004):
      1. Skeletal disease (such as but not limited to avascular necrosis, Erlenmeyer flask deformity, osteopenia or pathological fracture); **OR**
      2. Two or more of the following:
         a. Clinically significant hepatomegaly; **OR**
         b. Clinically significant splenomegaly; **OR**
         c. Hemoglobin at least 1.0 g/dL below lower limit of normal for age and sex; **OR**
         d. Platelet count less than or equal to 120,000 mm^3;

OR

II. Individual is less than 18 years of age with a diagnosis of **type 1** Gaucher disease and the following criteria are met:
   A. Documentation is provided that Type 1 Gaucher disease is confirmed by either (Kaplan, 2013; Wang, 2011):
      1. Deficiency in glucocerebrosidase enzyme activity as measured in the white blood cells or skin fibroblasts; **OR**
      2. Genotype testing indicates mutation of two alleles of the glucocerebrosidase genome; **AND**
   B. Individual has clinically significant manifestations of Gaucher disease (such as but not limited to hepatomegaly, splenomegaly, anemia, thrombocytopenia, skeletal disease or growth failure) (Andersson, 2005);

OR

III. Documentation is provided that individual is 18 years of age or older with a diagnosis of **type 3** Gaucher disease and the following criteria are met (Kaplan, 2013):
   A. Type 3 Gaucher disease is verified by genotype testing indicating mutation of two alleles of the glucocerebrosidase genome (Kaplan, 2013; Wang, 2011); **AND**
   B. Individual has clinically significant manifestations of Gaucher disease including (Andersson, 2005; Weinreb, 2004):
      1. Skeletal disease (such as but not limited to avascular necrosis, Erlenmeyer flask deformity, osteopenia or pathological fracture); **OR**
      2. Two or more of the following:
         a. Clinically significant hepatomegaly; **OR**
         b. Clinically significant splenomegaly; **OR**
         c. Hemoglobin at least 1.0 g/dL below lower limit of normal for age and sex; **OR**
         d. Platelet count less than or equal to 120,000mm^3; **AND**
   C. There are neurological findings consistent with type 3 Gaucher disease based on neurological evaluation including brain imaging [magnetic resonance imaging (MRI) or computed tomography (CT)] and electroencephalography (EEG) (Vellodi, 2009);

OR

IV. Documentation is provided that individual is less than 18 years of age with a diagnosis of **type 3** Gaucher disease and the following criteria are met (Kaplan, 2013):
   A. Type 3 Gaucher disease is verified by genotype testing indicating mutation of two alleles of the glucocerebrosidase genome (Kaplan, 2013; Wang, 2011); **AND**
   B. Individual has clinically significant manifestations of Gaucher disease (such as but not limited to hepatomegaly, splenomegaly, anemia, thrombocytopenia, skeletal disease or growth failure) (Andersson, 2005); **AND**

C. There are neurological findings consistent with type 3 Gaucher disease based on neurological evaluation including brain imaging [magnetic resonance imaging (MRI) or computed tomography (CT)] and electroencephalography (EEG) (Vellodi, 2009).

Continuation requests for enzyme replacement therapy for Gaucher disease (Cerezyme [imiglucerase], Elelyso [taliglucerase], Vpriv [velaglucerase]) may be approved if the following criterion is met:

I. There is clinically significant improvement in clinical signs and symptoms of disease (including but not limited to reduction of spleen volume, reduction of liver volume, resolution of anemia, resolution of thrombocytopenia, reduction in fatigue, improvement in skeletal manifestations).

Enzyme replacement therapy for Gaucher disease [Cerezyme (imiglucerase), Elelyso (taliglucerase) and Vpriv (velaglucerase)] may not be approved for the following:

I. Individuals with type 2 Gaucher disease; **OR**
II. Use in combination with another enzyme replacement therapy agent or substrate reduction therapy agent [Cerdelga (eliglustat), Zavesca (miglustat)] for the treatment of Gaucher disease; **OR**
III. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Enzyme Replacement Therapy for Gaucher Disease Quantity Limits

Drug	Limit
Cerezyme (imiglucerase) 400 unit vial	60 units/kg as frequently as every 2 weeks*
Elelyso (taliglucerase) 200 unit vial	60 units/kg as frequently as every 2 weeks
Vpriv (velaglucerase) 400 unit vial	60 units/kg as frequently as every 2 weeks
Override Criteria	
I. Requests for higher dosing or more frequent administration may be approved when the treating physician has indicated that it is necessary based on the individual's disease severity or lack of response.	
II. Individuals currently being treated on a stable dosage of Cerezyme may be switched to Elelyso or Vpriv at the previous Cerezyme dosage.	
III. For Cerezyme, may approve alternate dosing of up to three times weekly.	

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J1786	Injection, imiglucerase, 10 units [Cerezyme]
J3060	Injection, taliglucerase alfa, 10 units [ELELYSO]
J3385	Injection, velaglucerase alfa, 100 units [VPRIV]
S9357	Home infusion therapy, enzyme replacement intravenous therapy; (e.g., Imiglucerase); administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

ICD-10 Diagnosis

E75.22	Gaucher disease

Document History

Revised: 6/12/2023
Document History:

- 6/12/2023 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 6/13/2022 – Annual Review: Remove Cerezyme 200 unit vial as not available. Wording and formatting changes. Coding Reviewed: No changes.
- 07/26/2021 – Administrative update to add documentation.
- 06/14/2021 – Annual Review: No changes. Coding Reviewed: No changes.

- 06/8/2020 – Annual Review: Update ERT clinical criteria with the addition of continuation criteria. Wording and formatting changes. Coding Reviewed: No changes
- 09/23/2019 – Administrative update to add drug specific quantity limits.
- 06/10/2019 – Annual Review: No changes. Coding reviewed: No changes.
- 11/16/2018 – Annual Review: Initial P&T review of Enzyme Replacement Therapy for Gaucher Disease. Remove monotherapy requirement from approvable section as duplicative of may not be approved criteria. Remove glucocerebrosidase enzyme deficiency threshold. Standardize anemia definition throughout criteria as hemoglobin at least 1.0 g/dL below lower limit of normal for age and sex. Streamline criteria for clinically significant manifestations of disease. Streamline criteria for neurologic examination. Add substrate reduction therapy to the agents that may not be used in combination with enzyme replacement therapy. Wording and formatting updates for clarification and consistency. Add references for non-label based criteria elements. HCPCS and ICD-10 coding review: No changes.

References

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.