09-J0000-41

Original Effective Date: 04/15/02

Reviewed: 06/10/26

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Subject: Intravenous Enzyme Replacement Therapy for Gaucher Disease

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Position Statement	Dosage/ Administration	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Gaucher disease is characterized by a deficiency of ß-glucocerebrosidase activity, resulting in accumulation of glucocerebrosidase in tissue macrophages which become engorged and are typically found in the liver, spleen and bone marrow and occasionally in lung, kidney and intestine. Secondary hematologic sequelae include severe anemia and thrombocytopenia in addition to the characteristic progressive hepatosplenomegaly, skeletal complications, including osteonecrosis and osteopenia, with secondary pathological fractures. Some forms of Gaucher disease cause significant disability and can be fatal.

Symptoms of Gaucher disease include fatigue, prolonged bleeding, easy bruising, bone pain, and pathological fractures. Signs of Gaucher disease include an enlarged spleen and liver, severe anemia, abnormal pigmentation, bone lesions, and occasionally lung dysfunction. In more severe cases, toxic levels of glycolipids accumulate in the nervous system, causing neuronal loss.

There are three clinical subtypes of Gaucher disease: type 1, type 2, and type 3. Type 1 (or non-neuronopathic) is the most common and symptoms being early in life or in adulthood. Most cases have no neurological involvement and are not diagnosed until adulthood. The clinical severity of type 1 is variable with some individuals never becoming symptomatic and others developing crippling skeletal symptoms during childhood. In type 2 Gaucher disease (acute infantile neuropathic Gaucher disease), liver and spleen enlargement are apparent by 3 months of age and individuals usually die before the age of two. Last, type 3 (or chronic neuronopathic Gaucher disease), liver and spleen enlargement varies and signs of brain involvement such as seizures gradually become apparent. Major symptoms also include skeletal irregularities, eye movement disorders, respiratory problems and blood disorders.

The preferred treatment of type 1 Gaucher disease is enzyme replacement therapy (e.g., imiglucerase [Cerezyme®], alglucerase [Ceredase®], velaglucerase [Vpriv™], or taliglucerase [Elelyso™]), which increases the degradation of glucocerebroside in macrophages with resultant reduction in the manifestations of Gaucher disease. However, oral treatment is available with Eliglustat (Cerdelga®) and Miglustat (Zavesca®). Enzyme replacement therapy may ameliorate visceromegaly and hematologic abnormalities in type 2 Gaucher disease. However, the recombinant enzyme does not cross the blood brain barrier and there is no evidence that enzyme replacement therapy has reversed, stabilized, or

slowed the progression of neurological involvement. Enzyme replacement therapy is also used in Gaucher disease type 3.

Alglucerase (Ceredase) was the first drug approved by the U.S. Food and Drug Administration (FDA) for treatment of type 1 Gaucher disease. It was manufactured from human placental tissue and has since been withdrawn from the market due to the approval of similar drugs made with recombinant DNA technology.

Imiglucerase (Cerezyme) is an analogue of the human enzyme ß-glucocerebrosidase. It is FDA approved for long-term enzyme replacement therapy (ERT) for pediatric and adult patients with a confirmed diagnosis of type 1 or type 3 Gaucher disease that results in anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly.

Velaglucerase alfa (Vpriv) and taliglucerase alfa (Elelyso) are enzymes created by gene activation technology in human fibroblast cells. Both velaglucerase alfa and taliglucerase alfa are FDA approved for long-term ERT for patients with type 1 Gaucher disease and have orphan drug designation for this same indication.

POSITION STATEMENT:

Site of Care: If intravenous enzyme replacement therapy for Gaucher disease is administered in a hospital-affiliated outpatient setting, additional requirements may apply depending on the member's benefit. Refer to 09-J3000-46: Site of Care Policy for Select Specialty Medications.

NOTE: Imiglucerase (Cerezyme) and velaglucerase (Vpriv) are the preferred intravenous enzyme replacement therapy for Gaucher disease

Initiation of imiglucerase (Cerezyme), velaglucerase (Vpriv), or taliglucerase (Elelyso) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with **ONE** of the following:
    a. Type 1 Gaucher disease confirmed by either of the following:
        i. Genotype testing indicating a mutation of two alleles of the glucocerebrosidase genome – laboratory documentation must be provided
        ii. Glucocerebrosidase activity deficiency in the white blood cells/skin fibroblasts – laboratory documentation must be provided
    b. Type 3 Gaucher disease confirmed by **BOTH** of the following:
        i. Genotype testing indicating a mutation of two alleles of the glucocerebrosidase genome – laboratory documentation must be provided
        ii. Neurologic manifestations consistent with Type 3 Gaucher disease (e.g., abnormal eye movement, seizures) – documentation from the medical record must be provided
2. Drug will be used as monotherapy (i.e., not in combination with eliglustat [Cerdelga], miglustat [Zavesca], imiglucerase [Cerezyme], alglucerase [Ceredase], velaglucerase [Vpriv], or taliglucerase [Elelyso])
3. Member meets **ONE** of the following:
    a. Younger than 18 years of age **AND** has one or more of the following:
        i. Abdominal or bone pain
        ii. Documented growth failure not associated with other conditions
        iii. Cachexia
        iv. Exertional limitations or fatigue

v. Evidence of bone disease
vi. Hemoglobin at least 2 g/dL below lower limit of normal for age and gender
vii. Thrombocytopenia (platelet count less than 60,000)
viii. Documented abnormal bleeding episode

b. 18 years of age and older **AND** has **ONE OR MORE** of the following:
i. Hemoglobin at least 1.0 g/dL below lower limit of normal for age and gender
ii. Thrombocytopenia (platelet count less than 120,000)
iii. Clinically significant hepatomegaly
iv. Clinically significant splenomegaly
v. Evidence of bone disease other than Erlenmeyer flask deformity or mild osteopenia

4. Taliglucerase (Elelyso) requests only: Member has an inadequate response, contraindication, or intolerance to imiglucerase (Cerezyme) or velaglucerase (Vpriv) – documentation from the medical record must be provided
5. Dose does not exceed 60 units/kg IV every 2 weeks

Approval duration: 1 year

Continuation imiglucerase (Cerezyme), velaglucerase (Vpriv), or taliglucerase (Elelyso) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of Gaucher disease, **OR** the member has previously met all indication-specific criteria
2. Member demonstrates a clinical improvement in symptoms following initiation of imiglucerase, velaglucerase, or taliglucerase – documention from the medical record must be provided
3. Drug will be used as monotherapy (i.e., not in combination with eliglustat [Cerdelga], miglustat [Zavesca], imiglucerase [Cerezyme], alglucerase [Ceredase], velaglucerase [Vpriv], or taliglucerase [Elelyso])
4. Dose does not exceed 60 units/kg IV every 2 weeks

Approval duration: 1 year

DOSAGE / ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

Table 2

FDA-Approved Indications and Recommended Dosing				
Drug	**FDA-approved indication**	**Initial Dose**	**Usual Dosage**	**Comments**
Imiglucerase (Cerezyme)	Long-term ERT in Type 1 Gaucher disease	2.5 units/kg three times weekly to 60	60 units/kg IV every 2 weeks	Administer over 1-2 hours

		units/kg every 2 weeks		
Velaglucerase alfa (Vpriv)	Long-term ERT in Type 1 Gaucher disease	60 units/kg IV every 2 weeks	60 units/kg IV every 2 weeks	• Administer over 1 hour • Members currently treated with a stable dose of imiglucerase may be switched to the same dose of velaglucerase
Taliglucerase alfa (Elelyso)	Long-term ERT in Type 1 Gaucher disease	60 units/kg IV every 2 weeks	60 units/kg IV every 2 weeks	• Administer over 1-2 hours • Members currently treated with a stable dose of imiglucerase may be switched to the same dose of taliglucerase
ERT, Enzyme replacement therapy				

Table 3

Drug Availability	
Imiglucerase (Cerezyme)	• 200 unit powder for injection • 400 unit powder for injection
Velaglucerase (Vpriv)	400 unit powder for injection
Taliglucerase (Elelyso)	200 unit powder for injection

Dosage Adjustment: Specific guidelines for dosage adjustments in hepatic or renal impairment are not available; it appears that no dosage adjustments are needed.

PRECAUTIONS:

CONTRAINDICATIONS:

There are no known contraindications to therapy with imiglucerase, velaglucerase and taliglucerase; however, they should be used with caution in members with a known hypersensitivity to the product.

Allergic and Infusion Reactions: Infusion-related reactions (including allergic reactions) have been observed following administration of enzyme replacement therapy. The majority of the reactions were mild and dissipated over time. Slowing the infusion rate or pretreatment with antihistamines and/or corticosteroids may prevent subsequent reactions in those cases where symptomatic treatment was required.

Children

- The safe and effective use of imiglucerase has been established in children and adolescents age 2 to 16 years.
- The safe and effective use of velaglucerase has been established in children over the age of 4 years.
- The safety and efficacy of taliglucerase has been established in children 4 years of age and older.

Pregnancy and Lactation

- Imiglucerase is classified as Pregnancy Category C; there are no adequate and well-controlled studies in pregnant women.

- Taliglucerase and velaglucerase are classified as Pregnancy Category B; although there are no adequate and well-controlled studies in pregnant women, reproduction studies in pregnant rats and rabbits did not show impaired fertility or harm to the fetus. Taliglucerase or velaglucerase administration in pregnant women should only occur if clearly needed.
- Additionally, no human studies have investigated the effects of imiglucerase, taliglucerase in breast-fed infants.

BILLING/CODING INFORMATION:

HCPCS Coding:

J1786	Injection, imiglucerase, 10 units
J3060	Injection, taliglucerase alfa, 10 units
J3385	Injection, velaglucerase alfa, 100 units

ICD-10 Diagnosis Codes That Support Medical Necessity:

E75.22	Gaucher disease

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date. The Site of Care Policy for Select Specialty Medications does not apply to Medicare Advantage members.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

DEFINITIONS:

Gaucher disease: familial disorder of lipid metabolism resulting in an accumulation of abnormal glucocerebrosides in reticuloendothelial cells, and manifested clinically by hepatosplenomegaly, skin pigmentation, skeletal lesions, and pingueculae.

Hemoglobin: normal hemoglobin values vary, but in general the following table describes levels for different populations.

Normal Hemoglobin Values (g/dL) Ranges		
	Male	Female
Newborn	14.7 – 18.6	12.7 – 18.3
6 months to 2 years	10.3 – 12.4	10.4 – 12.4
2-6 years	10.5 – 12.7	10.7 – 12.7
6-12 years	11.0 – 13.3	10.9 – 13.3
12-18 years	11.5 – 14.8	11.2 – 13.6

Greater than 18 years	13.5 – 17.5	12 – 16

RELATED GUIDELINES:

Oral Therapy for Gaucher Disease, 09-J0000-76

OTHER:

None applicable.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/10/26.

GUIDELINE UPDATE INFORMATION:

04/15/02	Original Medical Coverage Guideline Developed.
01/01/06	CPT coding update, deleted expired codes: 90780, 90781, added new codes 90765 and 90766.
08/15/05	Revised and Updated: added Ceredase to the title, added chemical name to the subject, updated dosage/administration, deleted precautions, contraindications, updated when services are not covered, reimbursement information, updated ICD-9 Coding, references, and the related internet links.
09/15/06	Biennial review and updated references.
01/01/07	MCG revised to include Medicare Part D as program exception.
08/15/07	Reviewed guideline: Reformatted guideline, maintain current coverage and limitations, requested MPAF pxdx audit, added paragraph regarding Gaucher disease, updated internet links and updated references.
01/01/09	Annual HCPCS coding update: deleted 90765 and 90766; added 96365 and 96366.
08/15/09	Review and revision to guideline; consisting of changing the name and updating references.
06/15/10	Revision to guideline; consisting of adding new agent.
11/15/10	Review and revision to guideline; consisting of updating coding and references.
01/01/11	Revision to guideline; consisting of updating coding.
11/15/11	Review and revision to guideline; consisting of updating coding and references.
07/15/12	Revision to guideline; consisting of adding new product.
11/15/12	Review and revision to guideline; consisting of revising position statement, dosage/administration section, precautions/warnings section; updating references; adding contraindications section
07/15/13	Review and revision to guideline; consisting of revising position statement, updating references and coding.
10/15/13	Revision to guideline; consisting of removing algulcerase (Ceredase) from guideline (product is obsolete).
01/01/14	Revision to guideline; consisting of code update.
05/15/14	Review and revision to guideline; consisting of revising position statement to include continuation criteria.
11/15/14	Revision to guideline; consisting of description, position statement, dosing/administration
07/15/15	Review and revision to guidelines consisting of description, position statement, references.
11/01/15	Revision: ICD-9 Codes deleted.
01/15/16	Revision to guidelines; consisting of updating position statement.
07/15/16	Review and revision to guideline; consisting of updating position statement.
07/15/17	Review and revision to guideline; consisting of updating description and position statement.

07/15/18	Review and revision to guideline; consisting of updating references and position statement.
07/15/19	Review and revision to guideline; consisting of updating references and position statement.
11/11/19	Revision to guideline consisting of adding a reference to the Site of Care Policy for Select Specialty Medications and updating the Program Exceptions.
07/15/20	Review and revision to guideline; consisting of updating references.
06/15/22	Review and revision to guideline; consisting of updating Position Statement and updating references.
07/15/23	Review and revision to guideline; consisting of updating references.
07/15/25	Review and revision to guideline; consisting of updating references and position statement.
07/15/26	Review and revision to guideline; consisting of updating references.