Medicare Part B Gaucher Disease Prior Authorization

FDA APPROVED INDICATIONS AND DOSAGE[1-3]

Agent(s)	Indication(s)	Dosage
Cerezyme® (imiglucerase) Injection for intravenous use	For long-term enzyme replacement therapy of pediatric and adult patients with a confirmed diagnosis of Type 1 Gaucher disease that results in one or more of the following conditions: anemia, thrombocytopenia, bone disease, hepatomegaly or splenomegaly	Initial dosage range: 2.5 U/kg three times per week – 60 U/kg once every 2 weeks, the latter of which is the dosage for which the most data are available.[a] Administer as an intravenous infusion over 1-2 hours.
Elelyso® (taliglucerase alfa) Injection for intravenous use	For the treatment of patients 4 years and older with a confirmed diagnosis of Type 1 Gaucher disease	Recommended dosage: 60 units/kg every other week as a 60-120 minute intravenous infusion
Vpriv® (velaglucerase alfa) Injection for intravenous use	For long-term enzyme replacement therapy (ERT) for patients with type 1 Gaucher disease	Recommended dosage in patients 4 years and older:[b] 60 units/kg every other week as a 60-minute intravenous infusion

a - Disease severity may dictate that treatment be initiated at a relatively high dose or relatively frequent administration.
b - The efficacy and safety of Vpriv has not been established in pediatric patients younger than 4 years of age.

CLINICAL RATIONALE

Gaucher Disease

Gaucher disease (GD), the most common of the lysosomal storage disorders (LSDs), is a rare autosomal recessive metabolic disorder affecting only 1 in 40,000 in the general United States population.[5,7] Mutations in the *GBA* (glucocerebrosidase) gene cause reduced activity of the lysosomal enzyme glucocerebrosidase (also known as acid beta-glucosidase), resulting in the accumulation of harmful quantities of the glycolipid glucocerebroside (also known as glucosylceramide, or GLC) and other related sphingolipids. This multisystemic accumulation of GLC in various tissues, especially in lysosomes of macrophages, compromises the bone marrow, spleen, and liver, and less often the lungs, skin, kidneys, and heart.[4,5,7,9,10,11]

GD is classified into 3 clinical types, distinguished by their clinical features, management, and prognosis. However, as with most genetic diseases, there is a continuum of clinical findings and overlap within and between types, resulting in identification of additional subtypes.[5,7,8,10] GD Type 1 (GD1) is distinguished from GD Types 2 (GD2) and 3 (GD3) by the lack of characteristic involvement of the central nervous system (CNS).[4,5,7-9] As such, it is also known as non-neuronopathic GD.[4,5,7] In the United States, Europe, and Israel, 90% of GD patients have GD1, with a high carrier frequency in the Ashkenazi-Jewish population.[4,5,7-9] Age of onset for GD1 is variable, with some patients presenting between 12 and 24 months of age and others having no clinical signs until late adulthood.[4,5,7] Manifestation in the first or second decades of life typically results in more aggressive and severe symptoms than those manifesting at a later stage of life.[7] Presentation of symptoms

among patients with GD1 is variable. Splenomegaly is the most common symptom; hepatomegaly is also common, but the liver increases relatively less than the spleen. Other common presenting symptoms are anemia, thrombocytopenia, bone disease, and delayed growth.[4,5,7-9,11]

GD2 is an acute neuronopathic form of GD characterized by early onset, typically in the first year after birth. Neurologic complications are extensive and severe, with limited psychomotor development. Death occurs within the first 2 years of life, usually due to respiratory failure.[4,7,8] GD3 is the subacute or chronic neuronopathic form, has later onset than GD2, and has slower disease progression with patients typically surviving to second or third decades of life. The distinction between GD2 and GD3 is difficult.[4,5]

A diagnosis of GD should be considered in patients with unexplained anemia and easy bruising, particularly if they have enlargement of the spleen and liver.[4] Definitive diagnosis of GD can be confirmed by the finding of reduced glucocerebrosidase activity in leukocytes, fibroblasts, or other nucleated cells.[4,5,7,8,10,11] This enzyme assay test is typically known as BGL (beta-glucosidase leukocyte), and a finding of 15% or less of mean normal glucocerebrosidase enzyme activity is indicative of GD.[5,8] If BGL results are not conclusive and/or further confirmatory testing is desired, genetic testing is an option. Identification of two pathogenic alleles in the *GBA* gene can also determine diagnosis of GD.[4,5,8,10] The presence of neurologic complications has critical implications for prognosis and treatment and should be determined as soon as possible after diagnosis. Neuronopathic symptoms indicative of GD2 and GD3 include bulbar signs (e.g., stridor, strabismus, swallowing difficulty), pyramidal signs (e.g., opisthotonus, head retroflexion, spasticity, trismus), oculomotor apraxia, tonic-clonic seizures, myoclonic epilepsy, dementia, and ataxia. If not already performed as part of the diagnostic process, baseline measurement of hemoglobin level, platelet count, liver volume, and spleen volume should be documented.[5,7,8,11]

When possible, management of a patient with GD should occur with a multidisciplinary team at a Comprehensive Gaucher Treatment Center[8] (list of facilities nationwide available at www.gaucherdisease.org). Goals of treatment are elimination or improvement of symptoms, prevention of irreversible complications, and improvement in overall health and quality of life. An additional goal in children is optimization of growth.[4,6,9] Currently, two different therapeutic approaches for the treatment of GD1 are used: enzyme replacement therapy (ERT) [Cerezyme (imiglucerase), Vpriv (velaglucerase alfa), Elelyso (taliglucerase alfa)] and substrate reduction therapy (SRT) [Cerdelga (eliglustat), Zavesca (miglustat)].[4,6,8,9,10] ERT, intravenously administered, targets macrophages and increases the breakdown of accumulated glycolipids.[9] SRT, orally administered, reduces the amount of synthesized GLC to a level that can be effectively cleared by the mutated enzyme's residual activity.[6,8,9]

The decision to offer ERT or SRT in patients with GD1 is based upon disease severity and/or significant disease progression.[6,7,9,11] To begin treatment with ERT or SRT, clinically significant manifestations must be present. Thrombocytopenia of sufficient magnitude to justify initiation of treatment is defined by platelet counts less than 100,000 µL, as well as symptomatic presentation of splenomegaly, anemia, bone disease, and/or delayed growth.[4,5,7,8,9,10]

Safety

There are no FDA labeled contraindications for the target agents.[1-3]

References

1. Cerezyme prescribing information. Genzyme Corporation. December 2020.
2. Elelyso prescribing information. Pfizer Labs. November 2020.
3. Vpriv prescribing information. Shire Human Genetic Therapies, Inc. November 2019.
4. National Organization for Rare Disorders (NORD) – Physicians Guides. Gaucher Disease. Available at: https://rarediseases.org/physician-guide/gaucher-disease. Accessed November 2020.
5. Hughes D, Sidransky E, et al. Gaucher Disease: Pathogenesis, Clinical Manifestations, and Diagnosis. UpToDate. Last updated May 2019. Literature review current through October 2020. Accessed November 2020.
6. Hughes D, et al. Gaucher Disease: Treatment. UpToDate. Last updated April 2018. Literature review current through October 2020. Accessed November 2020.
7. Martins AM, Valadares ER, Porta G, et al. Recommendations on Diagnosis, Treatment, and Monitoring for Gaucher Disease. *J Pediatr*. 2009;155(4):S10-S18.
8. Pastores GM, Hughes DA. Gaucher Disease. July 2000 [Updated June 2018]. In: Adam MP, Ardinger HH, Pago RA, et al. Gene Reviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2019. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1269/. Accessed November 2020.
9. Biegstraaten M, Cox TM, Belmatoug N, et al. Management Goals for Type 1 Gaucher Disease: An Expert Consensus Document from the European Working Group on Gaucher Disease. *Blood Cells Mol Dis*. 2018;68:203-208.
10. Wang RY, Bodamer OA, Watson MS, et al. American College of Medical Genetics (ACMG) Work Group on Lysosomal Storage Diseases: Diagnostic Confirmation and Management of Presymptomatic Individuals. *Genet Med*. 2011 May;13(5):457-484.
11. Weinreb NJ, Aggio MC, Andersson HC, et al. Gaucher Disease Type 1: Revised Recommendations on Evaluations and Monitoring for Adult Patients. *Semin Hematol*. 2004;41(suppl 5):15-22.

Document History
Original Prime Standard Part B criteria, approved by P&T UM Committee 12/2021

Medicare Part B Gaucher Disease Prior Authorization

Coverage and policy application are contingent on National Coverage Determinations (NCD) and Local Coverage Determinations (LCD). An NCD or LCD that is applicable to the drug or product must be used in lieu of applicable medical necessity criteria. Also, please note that Prior Authorization criteria cannot be stricter than an NCD or LCD with specified step therapy requirements.

TARGET PREFERRED AGENT(S)	TARGET NON-PREFERRED AGENT(S)
Target preferred and non-preferred agent(s) to be determined client	Target preferred and non-preferred agent(s) to be determined client
Cerezyme (imiglucerase) **Elelyso** (taliglucerase alfa) **Vpriv** (velaglucerase alfa)	

Brand (generic)	GPI	Multisource Code	HCPCS Code
Cerezyme (imiglucerase)			
400 unit injection	82700050002120	M, N, O, or Y	J1786
Elelyso (taliglucerase alfa)			
200 unit injection	82700080102120	M, N, O, or Y	J3060
Vpriv (velaglucerase alfa)			
400 unit injection	82700085102120	M, N, O, or Y	J3385

CRITERIA FOR APPROVAL
Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. The requested agent is being used for ONE of the following:
    a. An FDA approved indication
    OR
    b. An indication in CMS approved compendia

    AND
2. If the client has preferred agents, then ONE of the following:
    a. The requested agent is the preferred agent
    OR
    b. Information has been provided that indicates the patient has been treated with the requested agent in the past 365 days
    OR
    c. There is documentation that the patient has had an ineffective treatment response to the active ingredient(s) of ALL preferred agent(s)
    OR
    d. The patient has a documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of ALL preferred agent(s)
    OR
    e. The prescriber has submitted documentation indicating ALL preferred agent(s) are likely to be ineffective or are likely to cause an adverse reaction or other harm to the patient

    AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
    AND

4. The requested quantity (dose) is within FDA labeled dosing or supported in compendia for the requested indication

Length of Approval: up to 12 months