Policy Number	RX501.190
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Enzyme Replacement Therapy for Gaucher Disease

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Related Policies (if applicable)
RX501.067 Enzyme Replacement Therapy for lysosomal storage disorders (excluding Gaucher and Pompe Disease)
RX501.189 Enzyme Replacement Therapy for Pompe Disease

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of care developed by: nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

Enzyme replacement therapy when utilized for the treatment of Gaucher Disease **may be considered medically necessary** for the specific indications noted under each of the following enzyme-replacements therapies:

Product	Criteria For Use
Imiglucerase (Cerezyme®)	Imiglucerase (Cerezyme®) **may be considered medically necessary** for adults and pediatrics with a diagnosis of non-central nervous system (CNS) manifestations of Type 1 **or** Type 3 Gaucher disease. Imiglucerase (Cerezyme®) **is considered experimental, investigational, and/or unproven** for all other non-Food and Drug Administration (FDA) approved indications.
Taliglucerase alfa (Elelyso®)	Taliglucerase alfa (Elelyso®) **may be considered medically necessary** for individuals 4 years of age or older with a confirmed diagnosis of Type 1 Gaucher disease. Taliglucerase alfa (Elelyso®) **is considered experimental, investigational, and/or unproven** for all other non-FDA approved indications.
Velaglucerase alpha (VPRIV®)	Velaglucerase alpha (VPRIV®) **may be considered medically necessary** for long-term enzyme replacement therapy for individuals 4 years of age or greater with Type 1 Gaucher disease. Velaglucerase alpha (VPRIV®) **is considered experimental, investigational, and/or unproven** for all other non-FDA approved indications.

Policy Guidelines

None.

Description

Lysosomal storage disorders are a group of inherited metabolic diseases that are characterized by the accumulation of waste products in the body's cells due to an enzyme deficiency. There are more than 70 lysosomal disorders and additional disorders continue to be identified. These individual disorders are rare inborn errors of metabolism, which results in the absence or deficiency of an enzyme which causes cellular deficiency. LSDs affect different parts of the body, including but not limited to the skeleton, brain, skin, heart, and central nervous system. As a group, lysosomal storage diseases are believed to have an estimated frequency of about 1 in 40,000-60,000. Although individual diseases are rare, the group together affects many people globally. (4, 5)

There is no cure for lysosomal storage disorders; however, enzyme-replacement therapy (ERT) can greatly improve the quality of life in select patients. The decision to start ERT for lysosomal disorders is based on the patient's symptoms or deterioration of those over time in each affected patient. Although ERT is not effective for neurologic symptoms, it may bring significant improvement in the quality of life of patients with severe clinical forms of neuronopathic Gaucher disease. (4, 5)

Gaucher Disease (Types I, II, and III)
Gaucher disease is the most common lysosomal storage disorder and occurs when both parents are carriers of the disease. Gaucher disease is caused by a deficiency in glucocerebrosidase, an enzyme that breaks down a fatty chemical in the body called glucocerebroside. Gaucher cells are normal scavenger cells called macrophages that become full of unprocessed glucocerebroside which accumulates in areas such as bone marrow, spleen, and liver resulting in organ inflammation and dysfunction. Depending on the type, Gaucher disease symptoms can include fatigue, anemia, bruising and bleeding, severe bone pain, fractures and enlarged spleen/liver. (6, 7)

There are 3 distinct types of Gaucher disease based upon the absence or presence and extent of neurological involvement:

- Gaucher disease Type 1: The most common form in Western countries. Symptoms include spleen and liver enlargement, bone problems, and bleeding problems due to low platelets/ abnormal clotting, and anemia. Brain development is normal.
- Gaucher disease Type 2: This type of Gaucher disease is rare and involves severe neurological (brain stem) abnormalities. It is usually fatal within the first 2 years, and it is currently untreatable because of severe, irreversible brain damage.
- Gaucher disease Type 3: This type of Gaucher disease is rare in the United States and Europe; however, it is the most common form of the disease worldwide. Gaucher disease Type 3 has a severity between Types 1 and 2, causing the same symptoms as Type 1 plus some neurological involvement. While patients typically have a shortened lifespan, some can live into their fifties with treatment. (6)

Non-central nervous system (CNS) manifestations of Type 1 or Type 3 Gaucher disease are treated with ERT to balance low levels of the enzyme glucocerebrosidase to break down the accumulation of glucocerebroside to minimize symptoms and the effect on various organs. (6, 7)

Regulatory Status
The following enzyme replacement therapies are U.S. Food and Drug Administration (FDA) approved for the treatment of specific types of Gaucher disease:

- Imiglucerase (Cerezyme®) is U.S. FDA approved for the treatment of non-central nervous system (CNS) manifestations of Type 1 or Type 3 Gaucher disease in adults and pediatric patients. (1)
- Taliglucerase alfa (Elelyso®) is U.S. FDA approved for the treatment of individuals 4 years and older with a confirmed diagnosis of Type 1 Gaucher disease. (2)
- Velaglucerase alpha (VPRIV®) was approved by the U.S. FDA in 2010 for long term ERT for individuals with Type 1 Gaucher disease. Safety and efficacy have not been established in individuals younger than 4 years of age. (3)

NOTE 2: Per the FDA labels, when receiving ERT, individuals should be monitored closely for hypersensitivity reactions, including anaphylaxis. Appropriate medical monitoring and support measures, including cardiopulmonary resuscitation equipment, should be readily available when

ERT is administered. Please refer to the U.S. FDA label for precautions for each individual ERT therapy.

Rationale

This policy is based on the U.S. Food and Drug Administration labeled indications for enzyme replacement therapy for Gaucher Disease.

Imiglucerase (Cerezyme®)
Study 1 was a randomized, double-blind, active-controlled clinical trial that enrolled 30 patients (17 male and 13 female) with Type 1 Gaucher disease. Patient ages ranged from 12 to 69 years, with a mean age of 38 years in the Cerezyme treatment group and mean age of 28 years in the alglucerase treatment group at baseline. The inclusion criteria required patients to have a hemoglobin of at least 1 g/dL below the lower limit of the normal range for their respective age and sex. Patients were randomized 1:1 to receive either Cerezyme 60 units/kg administered intravenously (IV) every other week or alglucerase for 6 months.

In Study 1, the primary efficacy parameters were an increase in hemoglobin concentration (at least 1 g/dL) and platelet count and a decrease in spleen and liver volume at 6 months. Efficacy results are shown in Table 1.

In Study 1, bone x-rays showed improvements in cortical thickness and lucencies in 7 of 11 Cerezyme treated patients.

Table 1: Change from Baseline to Month 6 in Clinical Efficacy Parameters in a Randomized, Double-Blind Active-Controlled Trial of Cerezyme Compared to Alglucerase in Patients 12 Years of Age and Older with Gaucher Disease Type 1 (Study 1)

Clinical Parameter		Cerezyme (N=15)	Alglucerase (N=15)	Difference (Cerezyme – Alglucerase) [95% CI]*
Hemoglobin concentration (g/dL)	Baseline	10.7	10.9	-
	Absolute Change from Baseline	1.9	1.6	0.3 [-0.6, 1.3]
Platelet count ($\times 10^3/mL^3$)	Baseline	68.5	74.2	-
	Absolute Change from Baseline	22.7	15.8	6.9 [-10.4, 24.1]
Liver volume (mL)	Baseline	2521	2788	-
	Absolute Change from Baseline	-310	-307	-3 [-246, 240]
	Percent Change from Baseline (%)	-11	-10	-1 [-9, 7]
Spleen volume (mL)	Baseline	2369	2603	-
	Absolute Change from Baseline	-902	-874	-28 [-652, 596]
	Percent Change from Baseline (%)	-35	-30	-5 [-14, 4]

CI: confidence interval; g/dL: grams per deciliter; mL: milliliter

* Confidence intervals were calculated using the t distribution (appropriate for small sample sizes) and the standard error of the difference in sample means (i.e., the pooled estimate of the common standard deviation, computed as the weighted average of the standard deviations in the two treatment groups); there was no evidence that the assumption of equal variances between the groups was violated.

In Study 2, an open-label extension study of Study 1, 29 patients with Type 1 Gaucher disease continued their assigned treatment for an additional 18 months. Patients were unblinded 3 months into Study 2 and those on alglucerase were allowed to cross-over to Cerezyme treatment. After total treatment duration of Cerezyme for 18-24 months, mean increase from baseline of Study 1 in hemoglobin was 2.4 g/dL, mean increase in platelet count was $40 \times 10^3/mm^3$, mean change in liver volume was -20%, and mean change in spleen volume was -57%.

The efficacy of Cerezyme for the treatment of non-CNS manifestations of Type 1 and Type 3 Gaucher disease was assessed in Study 3, an observational study, using data from the International Collaborative Gaucher Group (ICGG) Gaucher Disease Registry (NCT00358943). Study 3 included patients with Type 1 or Type 3 Gaucher disease who were treated with Cerezyme as initial therapy with an index clinical assessment and one or more follow-up clinical assessments. Study 3 was a baseline-controlled analysis in patients with Type 1 Gaucher disease (19 weeks to 87 years of age) and patients with Type 3 Gaucher disease (7 weeks to 54 years of age) who received Cerezyme IV as prescribed by their physicians (initiated treatment between 1992-2021). After approximately two years (1 to 3 years) of Cerezyme treatment in patients with Type 1 and 3 Gaucher disease, mean changes from baseline in the following measures showed improvement: hemoglobin, platelet count, liver volume, spleen volume, and height Z-score.

- Among 1,052 Type 1 Gaucher disease patients, mean baseline hemoglobin was 11.8 g/dL and mean increase from baseline was 1.5 g/dL (95% CI: 1.4, 1.5).
- Among 1,053 Type 1 Gaucher disease patients, mean baseline platelet count was $128 \times 10^3/mm^3$ and mean increase from baseline was $64 \times 10^3/mm^3$ (95% CI: 59.6, 67.9).
- Among 118 Type 3 Gaucher disease patients, mean baseline hemoglobin levels were 10 g/dL and mean increase from baseline was 1.8 g/dL (95% CI: 1.5, 2.1).
- Among 116 Type 3 Gaucher disease patients, mean baseline platelet count was $149 \times 10^3/mm^3$ and mean increase from baseline was $105 \times 10^3/mm^3$ (95% CI: 87.4, 122.4).

The 2-year summaries include measurements within 1 to 3 years after treatment initiation due to lack of predefined data collection timepoints in the registry.

Use in the Pediatric Population

The safety and effectiveness of Cerezyme for the treatment of non-CNS manifestations of Type 1 or Type 3 Gaucher disease have been established in pediatric patients. Use of Cerezyme for the treatment of non-CNS manifestations of Type 1 Gaucher disease is supported by evidence from adequate and well-controlled trials in adults and pediatric patients 12 years of age and older and additional safety and efficacy data from an observational study of Type 1 Gaucher disease in pediatric patients.

Use of Cerezyme for the treatment of non-CNS manifestations of Type 3 Gaucher disease is

supported by evidence from adequate and well-controlled trials in adults and pediatric patients 12 years of age and older with Type I Gaucher disease and additional safety and efficacy data from an observational study of Type 3 Gaucher disease in adults and pediatric patients.

Taliglucerase alfa (Elelyso®)

Clinical Trial in Adult Patients

The safety and efficacy of taliglucerase alfa (Elelyso) in the treatment of adult patients with Type 1 Gaucher disease was assessed in a 9-month, multi-center, double-blind, randomized trial (Trial 1) in 31 adult patients with Gaucher disease-related enlarged spleens (>8 times normal) and thrombocytopenia (<120,000/mm^3). Sixteen patients had enlarged livers, and ten patients had anemia at baseline. All patients were naïve to ERT. Patients with severe neurological symptoms were excluded from the trial. (2)

Patients were randomized to receive Elelyso at an IV dosage of either 30 units/kg (n=15; 50% of the recommended dosage) or 60 units/kg (the recommended dosage; n=16) every other week. After 9 months, 26 of the 31 patients continued in the blinded portion of the long-term extension trial for a total treatment duration of 24 months at the same IV dosage every other week. Twenty-three of those 26 patients continued open-label Elelyso treatment (30 or 60 units/kg given IV every other week) for an additional 12 months (total duration of Elelyso treatment was 36 months).

Baseline Demographics

In Trial 1, patients were 19 to 74 years of age (mean age 36 years), 48% were male, 97% were White and 29% and 71% were Hispanic/Latino and non-Hispanic/Latino, respectively.

Efficacy Results

Table 2 shows the baseline values and mean (standard deviation; SD) changes in clinical parameters (spleen volume, liver volume, platelet count, and hemoglobin) after 9 months of Elelyso treatment in Trial 1. Liver and spleen volumes were measured by magnetic resonance imaging (MRI) and are reported as percentage of body weight (%BW) and multiples of normal (MN). The observed reduction from baseline in spleen volume (the primary endpoint), was considered to be clinically meaningful in light of the natural history of untreated Gaucher disease.

Table 2: Mean (SD) Changes in Clinical Parameters from Baseline to 9 Months in Treatment-Naïve Adults with Type 1 Gaucher Disease Treated with Elelyso (N=31) (Trial 1)**

	Clinical Parameter	Elelyso 30 units/kg* (n=15) Mean (SD)	Elelyso 60 units/kg (n=16) Mean (SD)
Spleen Volume (%BW♯)	Baseline	3.1 (1.5)	3.3 (2.7)
	Month 9	2.2 (1.3)	2.1 (1.9)
	Change	-0.9 (0.4)	-1.3 (1.1)
Spleen Volume (MN♯)	Baseline	15.4 (7.7)	16.7 (13.4)
	Month 9	11.1 (6.3)	10.4 (9.4)
	Change	-4.5 (2.1)	-6.6. (5.4)
Liver Volume (%BW)	Baseline	4.2 (0.9)	3.8 (1.0)
	Month 9	3.6 (0.7)	3.1 (0.7)
	Change	-0.6 (0.5)	-0.6 (0.4)

Liver Volume (MN)	Baseline	1.7 (0.4)	1.5 (0.4)
	Month 9	1.4 (0.3)	1.2 (0.3)
	Change	-0.2 (0.2)	-0.3 (0.2)
Platelet Count (mm^3)	Baseline	75,320 (40,861)	65,038 (28,668)
	Month 9	86,747 (50,989)	106,531 (53,212)
	Change	11,427 (20,214)	41,494 (47,063)
Hemoglobin (g/dl)	Baseline	12.2 (1.7)	11.4 (2.6)
	Month 9	14.0 (1.4)	13.6 (2.0)
	Change	1.6 (1.4)	2.2 (1.4)

g/dl: grams per deciliter; kg: kilogram; mm^3: cubic millimeter; N: number.
*The recommended Elelyso dosage in treatment-naïve adult patients is 60 units/kg every other week. Elelyso 30 units/kg every other week is not a recommended dosage.
** SD = standard deviation
ǂ % BW = percentage of body weight
ǂǂ MN = multiples of normal

The following data are the changes in clinical parameters from baseline to Month 24 (including the 9-month initial period and the 15-month first long-term extension) for the 30 units/kg (n=12; 50% of the recommended dosage) and 60 units/kg (the recommended dosage; n=14) treatment groups, respectively: mean (SD) spleen volume (%BW) decreased by 1.4 (0.6) and 2.0 (2.0), in MN by 6.8 (3.0) and 10.2 (9.8); hemoglobin increased by 1.3 (1.7) g/dL and 2.4 (2.3) g/dL; liver volume (%BW) decreased by 1.1 (0.5) and 1.0 (0.7), in MN by 0.4 (0.2) and 0.4 (0.3) and platelet count increased 28,433 (31,996)/mm^3 and 72,029 (68,157)/mm^3 . The 23 patients who continued open-label Eleleyso treatment for additional 12 months demonstrated stability in these clinical parameters.

Clinical Trial in Pediatric Patients 16 Years of Age and Younger

The safety and efficacy of Elelyso in the treatment of pediatric patients with Type 1 Gaucher disease was assessed in a 12-month, multi-center, double-blind, randomized trial (Trial 2) in 9 treatment-naïve patients. Patients were randomized to receive Elelyso at an IV dosage of either 30 units/kg (n=4) (50% of the recommended dosage) or 60 units/kg (the recommended dosage; n=5) every other week. After 12 months, all 9 patients entered a blinded portion of the long-term extension trial (24-months of total treatment) where they continued treatment with Elelyso at the same dosage every other week.

Baseline Demographics

In Trial 2, patients were 2 to 13 years of age (mean age 8.1 years), 67% were male, 89% were White and 44% and 56% were Hispanic/Latino and non-Hispanic/Latino, respectively.

Efficacy Results

The following data in Trial 2 are the changes [median (Q1, Q3)] in clinical parameters from baseline to Month 12 for the 60 units/kg dose group (n=5): spleen volume decreased from 18.4 (14.2, 35.1) MN to 11.0 (8.3, 14.5) MN; hemoglobin increased from 11.1 (9.2, 11.3) g/dL to 11.7 (11.5, 12.9) g/dL;

liver volume decreased from 2.1 (2.0, 2.3) MN to 1.6 (1.5, 1.9) MN; platelet count increased from 80,000 (79,000, 87,000)/mm^3 to 131,000 (119,000, 215,000)/mm^3.

The following data are the changes [median (Q1, Q3)] in clinical parameters from baseline to Month 24 (including the initial 12-month period and the 12-month long-term extension) for the 60 units/kg dose group (n=5): spleen volume decreased by 19.0 (8.3, 41.2) MN; hemoglobin increased by 2.5 (1.9, 3.0) g/dL; liver volume decreased by 0.8 (0.6, 1.1) MN; and platelet count increased by 76,000 (67,000, 100,000)/mm^3.

Clinical Trial in Patients Switching from Imiglucerase Treatment to Elelyso

The safety and efficacy of Elelyso were assessed in 31 patients (26 adult and 5 pediatric patients) with Type 1 Gaucher disease who were switched from imiglucerase to Elelyso (Trial 3). Trial 3 was a 9-month, multi-center, open-label, single arm study in patients who had been receiving IV treatment with imiglucerase at dosages ranging from 9.5 units/kg to 60 units/kg every other week for a minimum of 2 years. Patients were required to be clinically stable and have a stable biweekly dosage of imiglucerase for at least 6 months prior to enrollment. Imiglucerase therapy was stopped, and treatment with Elelyso was administered every other week at the same number of units as each patient's previous imiglucerase dose (9.5 units/kg to 60 units/kg given IV every other week). If needed, adjustment of dosage was allowed during the study in order to maintain stability of clinical parameters (i.e., spleen volume, liver volume, platelet count, and hemoglobin).

- Eighteen of the 26 adult patients who completed the 9-month clinical trial continued treatment with Elelyso (9.5 units/kg to 60 units/kg given IV every other week) in an open-label extension trial for additional 27 months (total duration of Elelyso treatment was 36 months).
- Five of the pediatric patients who completed the 9-month trial continued open-label treatment with Elelyso (9.5 units/kg to 60 units/kg given IV every other week) for an additional 24 months (total duration of Elelyso treatment was 33 months).

Baseline Demographics

In Trial 3, patients were 6 to 66 years of age (mean age 42 years, including pediatric patients), 55% were male, 97% were White, and 16% and 84% were Hispanic/Latino and non-Hispanic/ Latino, respectively.

Efficacy Results

In Trial 3, at baseline, spleen volume was 5.2 (4.5) MN, liver volume was 1.0 (0.3) MN, platelet count was 161,137 (73,387)/mm^3, and hemoglobin was 13.5 (1.4) g/dL. Mean (SD) organ volumes and hematologic values remained stable through 9 months of ELELYSO treatment. After 9 months of ELELYSO treatment, spleen volume was 4.8 (4.6) MN, liver volume was 1.0 (0.2) MN, platelet count was 161,167 (80,820)/mm^3, and hemoglobin was 13.4 (1.5) g/dL. The Elelyso dosage remained unchanged in 30 of 31 patients. One patient required a dose increase at Week 24 (from 9.5 units/kg to 19 units/kg) for a platelet count of 92,000/mm^3 at Week 22, which subsequently increased to 170,000/mm^3 at Month 9.

During the 36-month period, 18 Elelyso-treated adult patients maintained stability in clinical parameters (spleen volume, liver volume, platelet count and hemoglobin); however, only 10 of 18 adult patients completed 27 months of Elelyso treatment in the extension trial and only 7 patients had their spleen and liver volumes assessed at 36 months.

During the 33-month period, the 5 Elelyso-treated pediatric patients demonstrated stability in these clinical parameters.

Use in the Pediatric Population

The safety and effectiveness of Elelyso for the treatment of pediatric patients 4 years of age and older with a confirmed diagnosis of Type 1 Gaucher disease has been established. The use of Elelyso for this indication is supported by evidence of effectiveness from adequate and well-controlled trials of Elelyso in adults, with additional pharmacodynamic data from 5 pediatric patients and pharmacokinetic data from 9 pediatric patients who participated in clinical trials. Data from 14 pediatric patients were included in the safety evaluation. The safety and effectiveness of Elelyso has not been established in patients less than 4 years of age.

Pediatric patients experienced a higher frequency of vomiting during Elelyso treatment (4 of 9 treatment-naïve patients) than adult patients, and this may be a symptom of hypersensitivity reaction. The frequencies of other adverse reactions were similar between pediatric and adult patients treated with Elelyso.

Velaglucerase alpha (VPRIV)

Clinical Trials of VPRIV for Gaucher Disease

The efficacy of VPRIV was assessed in three clinical trials in a total of 99 patients with type 1 Gaucher disease: 82 patients aged 4 years and older received VPRIV and 17 patients aged 3 years and older received imiglucerase. Studies I and II were conducted in patients who were not currently receiving Gaucher disease therapy. Study III was conducted in patients who were receiving imiglucerase treatment immediately before starting VPRIV. The long-term safety of VPRIV was assessed in Study IV, an open-label extension trial in a total of 93 patients with type 1 Gaucher disease ages 3 years and older. Patients who had completed Studies I to III were eligible to participate in Study IV. In Studies I through IV, VPRIV was administered IV over 60 minutes at a maximum dose of 60 Units/kg every other week. Doses above 60 Units/kg were not studied in these trials. (3)

Clinical Trials of VPRIV as Initial Therapy

Study I was a 12 month, randomized, double blind, parallel dose group, multinational trial in 25 patients aged 4 years and older with Gaucher disease related anemia and either thrombocytopenia or organomegaly. Patients were not allowed to have had disease-specific therapy for at least the previous 30 months; all but 1 had no prior therapy. The mean age was 26 years and 60% were male. Patients were randomized to receive VPRIV at a dose of either 45 units/kg (N=13) or 60 units/kg (N=12) every other week. The recommended starting dose in naïve patients is 60 Units/kg. The 45 Units/kg dosage is not recommended as a starting dose in naïve patients.

At baseline, mean hemoglobin concentration was 10.6 g/dL, mean platelet count was 97 x 10^9/L, mean liver volume was 3.6 % body weight (% BW), and mean spleen volume was 2.9 % BW.

For all studies, liver and spleen volumes were measured by MRI. The changes in clinical parameters after 12 months of treatment are shown in Table 3. The observed change from baseline in the primary endpoint, hemoglobin concentration, was considered to be clinically meaningful in the 60 units/kg dose, in light of the natural history of untreated Gaucher disease.

Table 3: Mean Change From Baseline to Month 12 For Clinical Parameters in Patients with Type 1 Gaucher Disease Initiating Therapy with VPRIV Given Every Other Week in Study I

Clinical Parameter	VPRIV 45 units/kg[#] N = 13 Mean ± SE	VPRIV 60 units/kg N = 12 Mean ± SE
Hemoglobin concentration change (g/dL)	2.4 ± 0.4[†]	2.4 ± 0.3*
Platelet count change (x 10^9/L)	41 ± 14[†]	51 ± 12[†]
Liver volume change (% BW)	-0.30 ± 0.29	-0.84 ± 0.33
Spleen volume change (% BW)	-1.9 ± 0.6[†]	-1.9 ± 0.5[†]

BW: body weight; SE = standard error of the mean; VPRIV: velaglucerase alpha.
[#] The recommended starting dose in naïve patients is 60 Units/kg. The 45 Units/kg dosage is not recommended as a starting dose in naïve patients.
[†] Statistically significant changes from baseline after adjusting for performing multiple tests.
* Primary study endpoint was hemoglobin concentration change in the 60 Units/kg group, p<0.001.

Study II was a 9-month, randomized, double blind, active-controlled (imiglucerase), parallel-group, multinational study in 34 patients aged 4 years and older. Patients were required to have Gaucher disease-related anemia and either thrombocytopenia or organomegaly. Patients were not allowed to have had disease specific therapy for at least the previous 12 months. The mean age was 30 years of age and 53% were female; the youngest patient who received VPRIV was age 4 years. Patients were randomized to receive either 60 units/kg of VPRIV (N=17) or 60 units/kg of imiglucerase (N=17) every other week.

At baseline, the mean hemoglobin concentration was 11.0 g/dL, mean platelet count was 171 x 10^9/L, and mean liver volume was 4.3 % BW. For the patients who had not had splenectomy (7 in each group) the mean spleen volume was 3.4 % BW. After 9 months of treatment, the mean absolute increase from baseline in hemoglobin concentration was 1.6 g/dL ± 0.2 (SE) for patients treated with VPRIV. The mean treatment difference in change from baseline to 9 months [VPRIV–imiglucerase] was 0.1 g/dL ± 0.4 (SE).

In both studies, examination of age and gender subgroups did not identify differences in response to VPRIV among these subgroups. The number of non-Caucasian patients in these studies was too small to adequately assess any difference in effects by race.

In Study IV treatment, naïve patients were administered VPRIV. Treatment-naïve patients continued to show improvements in clinical parameters (hemoglobin concentration, platelet count, liver volume, and spleen volume) compared with baseline for up to 60 months of treatment with ERT.

Clinical Trial in Patients Switching from Imiglucerase Treatment to VPRIV

Study III was a 12-month, open label, single-arm, multinational study in 40 patients aged 9 years and older who had been receiving treatment with imiglucerase at doses ranging between 15 units/kg to 60 units/kg for a minimum of 30 consecutive months. Patients also were required to have a stable biweekly dose of imiglucerase for at least 6 months prior to enrollment. The mean age was 36 years and 55% were female. Imiglucerase therapy was stopped, and treatment with VPRIV was administered every other week at the same number of units as the patient's previous imiglucerase dose. Adjustment of dosage was allowed by study criteria if needed to maintain clinical parameters.

Hemoglobin concentrations and platelet counts remained stable on average through 12 months of VPRIV treatment. After 12 months of treatment with VPRIV the median hemoglobin concentration was 13.5 g/dL (range: 10.8, 16.1) vs. the baseline value of 13.8 g/dL (range: 10.4, 16.5), and the median platelet count after 12 months was 174 x 10^9/L (range: 24, 408) vs. the baseline value of 162 x 10^9/L (range: 29, 399). No patient required dosage adjustment during the 12-month treatment period.

In Study IV, patients who had previously been receiving imiglucerase treatment were administered VPRIV. Patients previously treated with imiglucerase maintained stability in clinical parameters (hemoglobin concentration, platelet count, liver volume, and spleen volume) compared with baseline for up to 60 months of treatment with ERT.

Use in the Pediatric Population
The safety and effectiveness of VPRIV has been established for ERT in patients between 4 and 17 years of age with type 1 Gaucher disease. The use of VPRIV in this age group is supported by evidence from adequate and well-controlled studies of VPRIV in 74 adult patients and 20 pediatric patients. The safety and efficacy profiles were similar between pediatric and adult patients. The efficacy and safety of VPRIV has not been established in pediatric patients younger than 4 years of age.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J1786, J3060, J3385

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Labels:

1. Prescribing Label: Cerezyme® (imiglucerase) for injection, for intravenous use. January 2026. Available at: https://www.accessdata.fda.gov (accessed Feb. 24, 2026).
2. Prescribing Label: Elelyso® (taliglucerase alfa) for injection, for intravenous use. December 2025. Available at: https://www.accessdata.fda.gov (accessed Feb. 26, 2026).

3. Prescribing Label: VPRIV® (velaglucerase alfa) for injection, for intravenous use. July 2024. Available at: https://www.accessdata.fda.gov (accessed Feb. 26, 2026).

Other:

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Centers for Medicare & Medicaid Services

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare & Medicaid Services does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at https://www.cms.hhs.gov.

Policy History/Revision

Date	Description of Change
7/21/2026	New medical document. Enzyme replacement therapy when utilized for the treatment of Gaucher Disease may be considered medically necessary for the specific indications noted under each of the enzyme-replacements therapies in Coverage.