CEREZYME- imiglucerase injection, powder, lyophilized, for solution
Genzyme Corporation

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CEREZYME® safely and effectively. See full prescribing information for CEREZYME.

CEREZYME (imiglucerase) for injection, for intravenous use
Initial U.S. Approval: 1994

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

***See full prescribing information for complete boxed warning*.**

- **Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy. (5.1)**
- **Initiate CEREZYME in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. (5.1)**
- **If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue CEREZYME and immediately initiate appropriate medical treatment, including use of epinephrine. (5.1)**

RECENT MAJOR CHANGES

Indications and Usage (1)	1/2026
Dosage and Administration (2.3, 2.4, 2.5)	1/2026
Warnings and Precautions (5.1, 5.2)	1/2026

INDICATIONS AND USAGE

CEREZYME is a hydrolytic lysosomal glucocerebrosidase-specific enzyme indicated for the treatment of non-central nervous system (CNS) manifestations of Type 1 or Type 3 Gaucher disease in adults and pediatric patients. (1)

DOSAGE AND ADMINISTRATION

- Administer CEREZYME under the supervision of a healthcare provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis. (2.1)
- The recommended dosage is 2.5 units/kg three times a week to 60 units/kg once every two weeks administered intravenously. (2.2)
- Titrate the dosage based on disease severity and therapeutic goals for the patient. (2.2)
- See the full prescribing information for dosage modifications due to hypersensitivity reactions and/or IARs. (2.3)
- See the full prescribing information for preparation and administration instructions. (2.4, 2.5)

DOSAGE FORMS AND STRENGTHS

For injection: 400 units of imiglucerase as a lyophilized powder in a single-dose vial. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

Infusion-Associated Reactions (IARs): If a severe IAR occurs, discontinue CEREZYME immediately and initiate appropriate medical treatment. (5.2)

ADVERSE REACTIONS

- Adverse reactions reported in adults and pediatric patients include back pain, chills, dizziness, fatigue, headache, hypersensitivity reactions, nausea, pyrexia, and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme at 1-800-633-1610 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION.

FULL PRESCRIBING INFORMATION: CONTENTS*

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FULL PRESCRIBING INFORMATION

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with enzyme replacement therapies have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy.

Initiate CEREZYME in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue CEREZYME and immediately initiate appropriate medical treatment, including use of epinephrine. Inform patients of the symptoms of life-threatening hypersensitivity reactions, including anaphylaxis and to seek immediate medical care should symptoms occur *[see Warnings and Precautions (5.1)]*.

1 INDICATIONS AND USAGE

CEREZYME is indicated for the treatment of non-central nervous system (CNS) manifestations of Type 1 or Type 3 Gaucher disease in adults and pediatric patients.

2 DOSAGE AND ADMINISTRATION

2.1 Recommendations Prior to CEREZYME Treatment

Administer CEREZYME under the supervision of a healthcare provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis *[see Warnings and Precautions (5.1)]*.

Initiate CEREZYME in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment *[see Warnings and Precautions (5.1)]*.

For patients who experience hypersensitivity reactions to CEREZYME, premedicate with antihistamines and/or corticosteroids. Monitor patients for the occurrence of new hypersensitivity reactions *[see Warnings and Precautions (5.1)]*.

2.2 Recommended Dosage and Administration

Ensure physicians knowledgeable in the management of patients with Gaucher disease direct therapy with CEREZYME.

The recommended dosage of CEREZYME is 2.5 units/kg three times a week to 60 units/kg once every two weeks administered intravenously.

Titrate the dosage based on disease severity and therapeutic goals for the patient.

For adults and pediatric patients weighing greater than 20 kg, infuse the diluted CEREZYME solution over 1 to 2 hours *[see Dosage and Administration (2.5)]*.

For pediatric patients weighing 20 kg or less, infuse the diluted CEREZYME solution over 2 hours *[see Dosage and Administration (2.5)]*.

2.3 Dosage and Administration Modifications Due to Hypersensitivity Reactions and/or Infusion-Associated Reactions

If a *severe* hypersensitivity reaction (e.g., anaphylaxis) or a *severe* infusion-associated reaction (IAR) occurs, discontinue CEREZYME and immediately initiate appropriate medical treatment *[see Warnings and Precautions (5.1, 5.2)*].

If a *mild* or *moderate* hypersensitivity reaction or a *mild* or *moderate* IAR occurs, consider decreasing the infusion rate, temporarily stopping the infusion, and/or administering antihistamines, antipyretics, and/or corticosteroids [*see Warnings and Precautions (5.1, 5.2)*].

2.4 Preparation Instructions

Use aseptic technique during preparation.

Reconstitution

1. Determine the number of CEREZYME vials to be reconstituted based on the individual patient's dosage regimen and remove vial(s) from the refrigerator *[see Dosage and Administration (2.1)]*.
2. Reconstitute each vial of CEREZYME by slowly injecting 10.2 mL of Sterile Water for Injection, down the inside wall of each vial.
3. Roll and tilt the vial to allow the powder to dissolve completely. Visually inspect the reconstituted solution for particulate matter and discoloration. Discard if opaque particles or discoloration are observed. After reconstitution, each vial will yield CEREZYME at a concentration of 40 units/mL.
4. Withdraw the required volume of CEREZYME from the vial(s).

Dilution

1. Dilute the CEREZYME solution for infusion promptly with 0.9% Sodium Chloride Injection to a final volume that is calculated based on prescribed dose.
2. For CEREZYME administered at a dose of 60 units/kg, use the following final volumes (see Table 1).
   - For patients weighing between 1.5 kg and less than 6 kg, dilute CEREZYME to a final volume of 12 mL in a syringe for infusion.
   - For patients weighing between 6 kg and less than 13 kg, dilute CEREZYME to a final volume of 26 mL in a syringe for infusion.
   - For patients weighing between 13 kg and less than or equal to 20 kg, dilute CEREZYME to a final volume of 100 mL in an infusion bag.
   - For patients weighing greater than 20 kg and less than or equal to 100 kg, dilute CEREZYME to a final volume of 200 mL in an infusion bag.
   - For patients weighing greater than 100 kg, dilute CEREZYME to a final volume of 400 mL in an infusion bag.
3. If CEREZYME is prescribed at a dose lower than 60 units/kg, dilute the required total units of reconstituted CEREZYME (at a concentration of 40 units/mL) with 0.9% Sodium Chloride Injection to a final concentration between 6 units/mL and 30 units/mL inclusive. If the determined dose of CEREZYME translates into a total volume of 26 mL or less, administer using a syringe for infusion via a syringe pump.
4. For accuracy of dilution, if less than 2 mL of reconstituted CEREZYME (40 units/mL) is needed for the preparation of the determined dose, prepare a larger final volume

of CEREZYME for infusion initially maintaining the final concentration of the diluted CEREZYME solution between 6 units/mL to 30 units/mL. Subsequently, discard the excess volume and administer only the volume of CEREZYME solution corresponding to the prescribed dose.

5. Gently invert the syringe for infusion or the infusion bag to mix the solution. Throughout CEREZYME preparation, avoid vigorous shaking, agitation and foaming.

Vials are for single dose only. Discard any unused solution.

2.5 Administration Instructions

Visually inspect the diluted solution prior to administration of the final product for particulate matter and discoloration. Slight flocculation of protein particles (described as thin translucent fibers) may occur after dilution and does not affect the quality of the product.

Administer CEREZYME as an intravenous infusion with a 0.2 micron in-line low protein-binding filter.

Table 1: Total Infusion Volumes and Infusion Time for CEREZYME

Patient Weight	Total Infusion Volume*	Infusion Time	Maximum Infusion Rate
1.5 kg to < 6 kg	12 mL	2 hours	6 mL/hour
6 kg to < 13 kg	26 mL	2 hours	13 mL/hour
13 kg to ≤ 20 kg	100 mL	2 hours	50 mL/hour
> 20 kg to ≤ 100 kg	200 mL	1 to 2 hours	200 mL/hour
> 100 kg	400 mL	1 to 2 hours	400 mL/hour

* Final concentration of diluted CEREZYME solution is between 6 units/mL and 30 units/mL.

2.6 Storage and Handling

- If the reconstituted CEREZYME vial is not used immediately:
  - Refrigerate the reconstituted solution at 2°C to 8°C (36°F to 46°F) or store at room temperature at 20°C to 25°C (68°F to 77°F) for up to 12 hours.
- Refrigerate the diluted solution at 2°C to 8°C (36°F to 46°F) for up to 24 hours.

3 DOSAGE FORMS AND STRENGTHS

For injection: 400 units of imiglucerase as a white to off-white lyophilized powder in a single-dose vial for reconstitution.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions Including Anaphylaxis

Life-threatening hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with enzyme replacement therapies, including CEREZYME. In addition, other hypersensitivity reactions have included pruritus, flushing, urticaria, angioedema, chest discomfort, dyspnea, cough, cyanosis, tachycardia, and hypotension *[see Adverse Reactions (6.1)]*. Patients with antibody to imiglucerase have a higher risk of hypersensitivity reactions. Conversely, not all patients with symptoms of hypersensitivity have detectable IgG antibody. Consider periodic monitoring of patients during the first year of treatment for IgG antibody formation *[see Adverse Reactions (6.2)]*.

Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy. Administer CEREZYME under the supervision of a healthcare provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis. Initiate CEREZYME in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment.

If a *severe* hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue CEREZYME and immediately initiate appropriate medical treatment, including use of epinephrine. Consider the risks and benefits of re-administering CEREZYME following severe hypersensitivity reactions (including anaphylaxis). If the decision is made to re-administer CEREZYME, consider decreasing the infusion rate and administering antihistamines, antipyretics, and/or corticosteroids. Monitor patients for the occurrence of new signs and symptoms of a severe hypersensitivity reaction.

If a *mild* or *moderate* hypersensitivity reaction occurs, consider decreasing the infusion rate, temporarily stopping the infusion, and/or administering antihistamines, antipyretics, and/or corticosteroids.

Inform patients of the symptoms of life-threatening hypersensitivity reactions, including anaphylaxis and to seek immediate medical care should symptoms occur.

5.2 Infusion-Associated Reactions

Infusion-associated reactions (IARs) such as angioedema, pruritus, rash, urticaria, chest discomfort, chills, fatigue, infusion-site burning, infusion-site discomfort, infusion-site swelling, pyrexia and hypertension have been observed in patients treated with CEREZYME *[see Adverse Reactions (6.1)]*.

If a *severe* IAR occurs, discontinue CEREZYME and immediately initiate appropriate medical treatment. Consider the risks and benefits of re-administering CEREZYME following a severe IAR.

If a *mild* or *moderate* IAR occurs, consider decreasing the infusion rate, temporarily stopping the infusion, and/or administering antihistamines, antipyretics, and/or corticosteroids.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity Reactions Including Anaphylaxis *[see Warnings and Precautions*

(5.1)]
- Infusion-Associated Reactions *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trials and Postmarketing Experience

The following adverse reactions associated with the use of imiglucerase were identified in clinical studies or postmarketing reports. Because some of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

See Table 2 for adverse reactions occurring in adults and pediatric patients treated with CEREZYME in clinical trials and the postmarketing setting.

Table 2: Adverse Reactions in Adults and Pediatric Patients Treated with CEREZYME

	Adverse Reactions
Nervous system disorders	dizziness, headache
Cardiac disorders	tachycardia
Vascular disorders	cyanosis,* flushing,* hypotension,* hypertension*
Respiratory, thoracic and mediastinal disorders	cough,* dyspnea,* pneumonia, pulmonary hypertension
Gastrointestinal disorders	abdominal pain, diarrhea, nausea, vomiting
Immune system disorders	anaphylaxis,* hypersensitivity
Skin and subcutaneous tissue disorders	angioedema,* pruritus,* rash, urticaria*
Musculoskeletal and connective tissue disorders	back pain
General disorders and administration site conditions	chest discomfort,* chills, fatigue, infusion-site burning, infusion-site discomfort, infusion-site swelling, pyrexia

* Signs and symptoms suggestive of hypersensitivity reactions including anaphylaxis *[see Warnings and Precautions (5.1)]* and other infusion-associated reactions *[see Warnings and Precautions (5.2)]*.

6.2 Immunogenicity

The observed incidence of anti-drug antibodies (ADA) is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of ADA in the studies described below with the incidence of ADA in other studies, including those of CEREZYME or of other imiglucerase products.

Approximately 15% of patients treated and tested to date have developed IgG antibody to CEREZYME during the first year of therapy. Patients who developed IgG antibody did so largely within 6 months of treatment and rarely developed antibodies to CEREZYME after 12 months of therapy. Approximately 46% of patients with detectable IgG antibodies experienced symptoms of hypersensitivity. Patients with antibody to CEREZYME have higher risk of hypersensitivity reaction *[see Warnings and Precautions (5.1)]*. Patients who developed IgG antibody to CEREZYME had increased elimination

half-life compared to patients without antibody *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to CEREZYME during pregnancy. Pregnant women exposed to CEREZYME and health care providers are encouraged to contact the Gaucher patient registry at 1-800-745-4447, extension 15500 or visit www.registrynxt.com.

Risk Summary

Available data on more than 500 pregnancies from the international Gaucher Disease registry, postmarketing reports, published observational studies and case reports with CEREZYME or non–US-licensed imiglucerase use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are risks associated with symptomatic Type I Gaucher disease in pregnancy *(see Clinical Considerations)*. No animal reproduction studies have been conducted with imiglucerase.

The estimated background risk of major birth defects and miscarriage in the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

Pregnancy may exacerbate existing Type 1 Gaucher disease symptoms or result in new disease manifestations. Untreated symptomatic Type 1 Gaucher disease may lead to complications during pregnancy, including hepatosplenomegaly, which can interfere with the normal growth of a pregnancy and thrombocytopenia, which can lead to excessive bleeding.

8.2 Lactation

Risk Summary

Available published literature suggests a small amount of imiglucerase is present in breast milk immediately following an infusion of imiglucerase. Published case reports and postmarketing reports of breastfed infants have not reported adverse effects due to CEREZYME exposure. There are no data available on the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CEREZYME and any potential adverse effects on the breastfed infant from imiglucerase or from the underlying maternal condition.

Lactating women with Gaucher disease treated with CEREZYME should be encouraged to enroll in the Gaucher patient registry *[see Use in Specific Populations (8.1)]*.

8.4 Pediatric Use

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 *[see Adverse Reactions (6.1) and Clinical Studies (14)]*.

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 *[see Adverse Reactions (6.1) and Clinical Studies (14)]*.

8.5 Geriatric Use

Among the patients with Type 1 Gaucher disease in Study 3 *[see Clinical Studies (14)]* who had hemoglobin or platelet count measurements 1 to 3 years after initiating CEREZYME (n = 1,053), 6% of patients were 65 and over and 1% were 75 and over. No overall differences in effectiveness of CEREZYME were observed between patients 65 years of age and older and younger adult patients with Type 1 Gaucher disease.

The safety evaluation for patients 65 years of age and older with Type 1 Gaucher disease was conducted using data from a pharmacovigilance database that collected individual case safety reports and did not reveal new safety findings. Clinical studies of CEREZYME did not include sufficient numbers of patients 65 years of age and older to detect differences in safety between older and younger adult patients with Type 1 Gaucher disease.

Clinical studies of CEREZYME did not include sufficient numbers of patients 65 years of age and older to detect differences in efficacy and safety between older and younger adult patients with Type 3 Gaucher disease.

11 DESCRIPTION

Imiglucerase is a hydrolytic lysosomal glucocerebrosidase-specific enzyme. It is an analogue of the human enzyme b-glucocerebrosidase (b-D-glucosyl-N-acylsphingosine glucohydrolase, E.C. 3.2.1.45), produced by recombinant DNA technology using mammalian cell culture (Chinese hamster ovary). Purified imiglucerase is a monomeric glycoprotein of 497 amino acids, containing 4 N-linked glycosylation sites (Mr=60,430). Imiglucerase differs from placental glucocerebrosidase by one amino acid at position 495, where histidine is substituted for arginine. The oligosaccharide chains at the glycosylation sites have been modified to terminate in mannose sugars. The modified carbohydrate structures on imiglucerase are somewhat different from those on placental glucocerebrosidase.

CEREZYME (imiglucerase) for injection is intended for intravenous use. It is supplied as a sterile, nonpyrogenic, white to off-white lyophilized powder for reconstitution with Sterile Water for Injection, USP. Each single-dose vial contains 424 units imiglucerase, mannitol (340 mg), polysorbate 80, NF (1.06 mg), and sodium citrates: disodium hydrogen citrate

(36 mg) and trisodium citrate (104 mg).

An enzyme unit (U) is defined as the amount of enzyme that catalyzes the hydrolysis of 1 micromole of the synthetic substrate para-nitrophenyl-b-D-glucopyranoside (pNP-Glc) per minute at 37°C. Reconstituted solutions have a pH of approximately 6.1.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Gaucher disease is characterized by a deficiency of β-glucocerebrosidase activity, which results in accumulation of glucocerebroside in various tissues including liver, spleen, and bone marrow. The mannose sugars on imiglucerase mediate binding to and internalization by cells including macrophages. CEREZYME catalyzes the hydrolysis of glucocerebroside to glucose and ceramide.

12.2 Pharmacodynamics

No formal pharmacodynamic studies have been conducted with CEREZYME.

12.3 Pharmacokinetics

During one-hour intravenous infusions of four doses (7.5, 15, 30, 60 units/kg) of CEREZYME, steady-state enzymatic activity was achieved by 30 minutes. Following infusion, the half-life of plasma enzymatic activity ranged from 3.6 to 10.4 minutes. Plasma clearance ranged from 9.8 to 20.3 mL/min/kg (mean ± SD, 14.5 ± 4.0 mL/min/kg). The volume of distribution corrected for weight ranged from 0.09 to 0.15 L/kg (mean ± SD, 0.12 ± 0.02 L/kg). These variables do not appear to be influenced by dose or duration of infusion. However, only one or two patients were studied at each dose level and infusion rate.

Antidrug Antibody Effects on Pharmacokinetics

In patients who developed IgG antibody to CEREZYME, an apparent effect on serum enzyme levels resulted in diminished volume of distribution and clearance and increased elimination half-life compared to patients without antibody *[see Adverse Reactions (6.2)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long-term studies in animals to evaluate carcinogenic potential have not been performed with imiglucerase.

Mutagenesis

Imiglucerase was negative in the Ames test.

Impairment of Fertility

An animal fertility study was not performed. No histopathological findings on reproductive organs were observed in 13-week toxicity studies conducted in rats and

monkeys.

14 CLINICAL STUDIES

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 a mean age of 28 years in the alglucerase treatment group at baseline. The inclusion criteria required patients to have a hemoglobin level 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 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 3.

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

Table 3: 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 ($\times 10^3/mm^3$)	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]

* 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 intravenously 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 $128\times10^3/mm^3$ and mean increase from baseline was $64\times10^3/mm^3$ (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 $149\times10^3/mm^3$ and mean increase from baseline was $105\times10^3/mm^3$ (95% CI: 87.4, 122.4).

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

16 HOW SUPPLIED/STORAGE AND HANDLING

CEREZYME (imiglucerase) for injection is supplied as a white to off-white lyophilized powder in a carton containing one single-dose vial: NDC 58468-4663-1. Each vial contains 400 units of imiglucerase. CEREZYME does not contain any preservatives.

Store refrigerated at 2°C to 8°C (36°F to 46°F).

For storage of reconstituted and diluted solution *[see Dosage and Administration (2.2)]*.

17 PATIENT COUNSELING INFORMATION

Hypersensitivity Reactions Including Anaphylaxis and Infusion-Associated Reactions

Advise patients and caregivers that life-threatening hypersensitivity reactions, including anaphylaxis, and IARs may occur with CEREZYME treatment.

Advise patients and caregivers that anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy.

Inform patients and caregivers of the symptoms of life-threatening hypersensitivity reactions, including anaphylaxis, and IARs and to seek immediate medical care should symptoms occur *[see Warnings and Precautions (5.1, 5.2)]*.

Patient Registry

Inform patients and caregivers that the Gaucher patient registry has been established in order to better understand the variability and progression of Gaucher disease and to continue to monitor and evaluate long-term treatment effects of CEREZYME. A pregnancy sub-registry will also monitor the effects of CEREZYME on pregnant women and their offspring *[see Use in Specific Populations (8.1)]*. Encourage patients and caregivers to participate in the Gaucher patient registry. Advise patients that their participation is voluntary and may involve long-term follow-up. For information regarding the registry program, visit www.registrynxt.com or call 1-800-745-4447, extension 15500.

Manufactured by:
Genzyme Corporation
Cambridge, MA 02141
A SANOFI COMPANY
U.S. License Number: 1596

CEREZYME is a registered trademark of Genzyme Corporation.

PRINCIPAL DISPLAY PANEL - 400 Unit Vial Carton

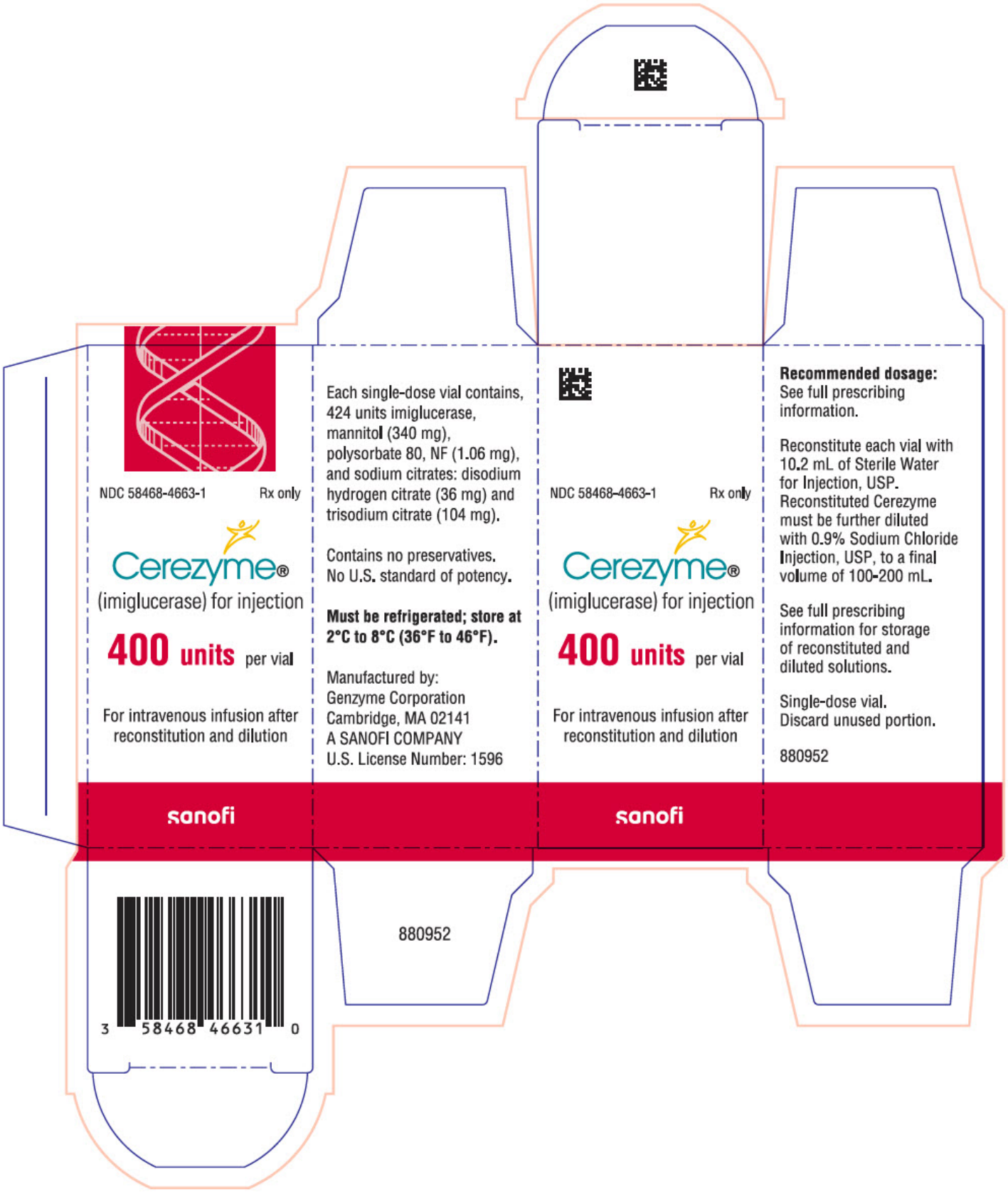
NDC 58468-4663-1
Rx only

Cerezyme®
(imiglucerase) for injection

400 units per vial

For intravenous infusion after
reconstitution and dilution

sanofi



CEREZYME

imiglucerase injection, powder, lyophilized, for solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:58468-4663
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IMIGLUCERASE (UNII: Q6U6J48BWY) (IMIGLUCERASE - UNII:Q6U6J48BWY)	IMIGLUCERASE	40 U in 1 mL

Inactive Ingredients

Ingredient Name	Strength
MANNITOL (UNII: 3OWL53L36A)	32.08 mg in 1 mL
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	9.81 mg in 1 mL
DISODIUM HYDROGEN CITRATE (UNII: 6FO62KCQ7A)	3.4 mg in 1 mL
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	0.1 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58468-4663-1	1 in 1 CARTON	05/23/1994	
1		10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA020367	05/23/1994	

Labeler - Genzyme Corporation (025322157)

Registrant - Genzyme Ireland Limited (985127419)

Establishment

Name	Address	ID/FEI	Business Operations
Genzyme Ireland Limited		985127419	ANALYSIS(58468-4663) , MANUFACTURE(58468-4663) , PACK(58468-4663) , LABEL(58468-4663)

Establishment

Name	Address	ID/FEI	Business Operations
Genzyme Corporation		050424395	PACK(58468-4663) , LABEL(58468-4663)

Establishment

Name	Address	ID/FEI	Business Operations

Charles River Laboratories, Inc.		078495006	ANALYSIS(58468-4663)

Establishment

Name	Address	ID/FEI	Business Operations
Eurofins Biopharma Product Testing Ireland Limited		238239933	ANALYSIS(58468-4663)

Establishment

Name	Address	ID/FEI	Business Operations
Genzyme Corporation		117450412	ANALYSIS(58468-4663) , MANUFACTURE(58468-4663) , API MANUFACTURE(58468-4663)

Establishment

Name	Address	ID/FEI	Business Operations
Genzyme Corporation		968302658	ANALYSIS(58468-4663)

Establishment

Name	Address	ID/FEI	Business Operations
Genzyme Corporation		034378252	ANALYSIS(58468-4663) , MANUFACTURE(58468-4663) , API MANUFACTURE(58468-4663)

Establishment

Name	Address	ID/FEI	Business Operations
Sanofi S.r.l.		338454274	ANALYSIS(58468-4663) , MANUFACTURE(58468-4663) , PACK(58468-4663) , LABEL(58468-4663)