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

ELELYSO® (taliglucerase alfa) for injection, for intravenous use
Initial US Approval: 2012

----------RECENT MAJOR CHANGES----------
Dosage and Administration, Administration Instructions (2.3) 8/2022

----------INDICATIONS AND USAGE----------
ELELYSO is a hydrolytic lysosomal glucocerebroside-specific enzyme indicated for the treatment of patients 4 years and older with a confirmed diagnosis of Type 1 Gaucher disease (1).

----------DOSAGE AND ADMINISTRATION----------
Recommended Dosage in Patients 4 Years and Older (2.1):
- Treatment-naïve: 60 units/kg administered every other week as a 60 to 120-minute intravenous infusion.
- Patients switching from imiglucerase: Begin ELELYSO at the same unit/kg dose as the patient's previous imiglucerase dose. Administer ELELYSO every other week as a 60 to 120 minute intravenous infusion. Dosage adjustments can be based on achievement and maintenance of each patient's therapeutic goals.

Preparation and Administration (2.2, 2.3):
- Reconstitute, dilute and administer under the supervision of a healthcare professional.
- See Full Prescribing Information for complete instructions.

----------DOSAGE FORMS AND STRENGTHS----------
For injection: 200 units lyophilized powder in a single-dose vial for reconstitution (3)

----------CONTRAINDICATIONS----------
None (4)

----------WARNINGS AND PRECAUTIONS----------
Hypersensitivity Reactions Including Anaphylaxis: Observe patients during and after the infusion; immediately discontinue infusion if anaphylaxis occurs and initiate appropriate treatment. Reduction in the infusion rate and/or pre-medication may prevent subsequent reactions (5.1, 6.3).

----------ADVERSE REACTIONS----------
The most common adverse reactions are:
- Treatment-Naïve Adults (≥5%): headache, arthralgia, fatigue, nausea, dizziness, abdominal pain, pruritus, flushing, vomiting, urticaria (6.1).
- Patients Switched from Imiglucerase, after 9 Months on Treatment (≥10%): arthralgia, headache, pain in extremity (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ELELYSO is indicated for the treatment of patients 4 years and older with a confirmed diagnosis of Type 1 Gaucher disease.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage in Patients 4 Years and Older

Treatment-naïve patients: The recommended dosage of ELELYSO for long-term treatment is 60 units/kg (based on actual body weight) administered every other week as a 60 to 120 minute intravenous infusion.

Patients switching from imiglucerase: Patients currently being treated with imiglucerase for Type 1 Gaucher disease can be switched to ELELYSO. Patients previously treated on a stable dosage of imiglucerase are recommended to begin treatment with ELELYSO at that same units/kg dosage when they switch from imiglucerase to ELELYSO. Administer ELELYSO for long-term treatment every other week as a 60 to 120 minute intravenous infusion. Dosage adjustments can be made based on achievement and maintenance of each patient's therapeutic goals *[see Clinical Studies (14.2)]*.

2.2 Preparation Instructions

ELELYSO should be reconstituted, diluted, and administered under the supervision of a healthcare professional.

Each vial of ELELYSO provides 200 units of taliglucerase alfa and is intended for one-time use and for only one patient. The reconstitution and dilution steps must be completed using aseptic technique.

ELELYSO should be reconstituted with Sterile Water for Injection, USP and diluted with 0.9% Sodium Chloride Injection, USP, to a final volume of 100 mL to 200 mL, and administered by intravenous infusion.

Prepare ELELYSO according to the following steps. Use aseptic technique.

a. Determine the number of vials to be reconstituted based on the patient's weight and the recommended dose of 60 units/kg, using the following calculations (1-3):

   (1) Total dose in units = Patient's weight (kg) x dose (units/kg)

   (2) Total number of vials = Total dose in units divided by 200 units/vial

   (3) Round up to the next whole vial.

b. Remove the required number of vials from the refrigerator. Do not leave these vials at room temperature longer than 24 hours prior to reconstitution. Do not heat or microwave these vials.

c. Reconstitute each vial of ELELYSO with 5.1 mL of Sterile Water for Injection, USP to yield a reconstituted product with a concentration of 40 units/mL and an extractable volume of 5 mL. Upon reconstitution, mix vials gently. DO NOT SHAKE. Prior to further dilution, visually inspect the solution in the vials; the solution should be clear and colorless. Do not use if the solution is discolored or if foreign particulate matter is present.

d. Withdraw the calculated dose of drug from the appropriate number of vials and dilute with 0.9% Sodium Chloride Injection, USP, to a final volume of 100 to 200 mL.
   i. For pediatric patients, a final volume of 100 to 120 mL should be used.
   ii. For adult patients, a final volume of 130 to 150 mL may be used. However, if the volume of reconstituted product alone is equal to or greater than 130 to 150 mL, then the final volume should not exceed 200 mL.

e. Mix gently. DO NOT SHAKE. Since this is a protein solution, slight flocculation (described as translucent fibers) occurs occasionally after dilution.

f. Discard any unused solution.

Storage and Handling of the Reconstituted and Diluted Solution

- If the reconstituted ELELYSO vial is not used immediately, store refrigerated at 2 °C to 8° C (36 °F to 46 °F) for up to 24 hours under protection from light or room temperature at 20 °C to 25 °C (68 °F to 77 °F) for up to 4 hours without protection from light.
- If the diluted solution is not administered immediately, store refrigerated at 2 °C to 8 °C (36 °F to 46 °F) for up to 24 hours under protection from light.
- Storage of the reconstituted product and the diluted product should not exceed a total of 24 hours.
- Do not freeze.

2.3 Administration Instructions

After reconstitution and dilution, the preparation should be administered via intravenous infusion over a minimum of 60 minutes and filtered through an in-line low protein-binding 0.2 µm filter.

- For pediatric patients weighing less than 30 kg (based on actual body weight): An infusion rate of 1 mL/minute should be used.
- For pediatric patients weighing greater than or equal to 30 kg (based on actual body weight): An initial infusion rate of 1 mL/minute should be used. After tolerability to ELELYSO is established, the infusion rate may be increased to a maximum of 2 mL/minute.
- For adult patients: An initial infusion rate of 1.2 mL/minute should be used. After tolerability to ELELYSO is established, the infusion rate may be increased to a maximum of 2.2 mL/minute.

3 DOSAGE FORMS AND STRENGTHS

For injection: 200 units 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

Serious hypersensitivity reactions, including anaphylaxis, have occurred in some patients treated with ELELYSO. In clinical trials, 2 of 72 (3%) patients treated with ELELYSO experienced signs and symptoms consistent with anaphylaxis. Signs and symptoms of these patients included urticaria, hypotension, flushing, wheezing, chest tightness, nausea, vomiting, and dizziness. These reactions occurred during ELELYSO infusion.

In clinical trials with ELELYSO, 21 of 72 (29%) patients experienced hypersensitivity reactions, including anaphylaxis. Signs and symptoms of hypersensitivity reactions included pruritus, angioedema, flushing, erythema, rash, nausea, vomiting, cough, chest tightness, and throat irritation. These reactions have occurred up to 3 hours after the start of infusion *[see Adverse Reactions (6.1)]*.

Due to the potential for anaphylaxis, appropriate medical support should be readily available when ELELYSO is administered. Observe patients closely for an appropriate period of time after administration of ELELYSO, taking into account the time to onset of anaphylaxis seen in clinical trials. Inform patients of the signs and symptoms of anaphylaxis, and instruct them to seek immediate medical care should signs and symptoms occur. If anaphylaxis occurs, discontinue ELELYSO immediately, and initiate appropriate medical treatment.

Management of hypersensitivity reactions should be based on the severity of the reaction and includes slowing or temporary interruption of the infusion and/or administration of antihistamines, antipyretics, and/or corticosteroids for mild reactions. Pretreatment with antihistamines and/or corticosteroids may prevent subsequent hypersensitivity reactions. Patients were not routinely premedicated prior to infusion of ELELYSO during clinical studies. If severe hypersensitivity reactions occur, immediately stop the infusion of ELELYSO and initiate appropriate treatment.

Consider the risks and benefits of re-administering ELELYSO in patients who have experienced a severe reaction associated with ELELYSO. Caution should be exercised upon rechallenge, and appropriate medical support should be readily available *[see Adverse Reactions (6.3)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials of ELELYSO as Initial Therapy

- Clinical Trial in Patients 19 Years and Older

  The safety of ELELYSO at dosages of either 30 units/kg (n=16) or 60 units/kg (n=16) every other week was assessed in 32 adult treatment-naïve patients (aged 19 to 74 years) with Type 1 Gaucher disease in a 9-month double-blind, randomized clinical trial.

Table 1: Adverse Reactions in ≥5% of Treatment-Naïve Adult Patients Treated with ELELYSO

Preferred Term	Treatment-Naïve Adults (N=32) n (%)
Headache	6 (19)
Arthralgia	4 (13)
Fatigue	3 (9)
Nausea	3 (9)
Dizziness	3 (9)
Abdominal pain	2 (6)
Pruritus	2 (6)
Flushing	2 (6)
Vomiting	2 (6)
Urticaria	2 (6)

- Clinical Trial in Patients 16 Years and Younger

The safety of ELELYSO at dosages of either 30 units/kg (n=4) or 60 units/kg (n=5) every other week was assessed in 9 pediatric treatment-naïve patients (aged 2 to 13 years) with Type 1 Gaucher disease in a 12-month randomized clinical trial.

The most common adverse reaction (≥10%) was vomiting, which occurred in 4 of 9 patients. Two patients developed hypersensitivity reactions; one patient experienced severe vomiting and gastrointestinal inflammation, and 1 experienced mild throat irritation and chest discomfort. Both patients responded to treatment with antihistamines and continued ELELYSO treatment.

Clinical Trial in Patients Switching from Imiglucerase Treatment to ELELYSO

The safety of ELELYSO was assessed in 31 patients (26 adult and 5 pediatric patients), ages 6 to 66 years old, with Type 1 Gaucher disease who had previously been receiving treatment with imiglucerase for a minimum of 2 years. ELELYSO was administered for 9 months at the same number of units as each patient's previous imiglucerase dose.

Table 2: Adverse Reactions in ≥10% of Patients Switched from Imiglucerase to ELELYSO (after 9 months on treatment)

Preferred Term	Patients Switched from Imiglucerase (N=31; 26 adults and 5 children) n (%)
Arthralgia	4 (13)
Headache	4 (13)
Pain in extremity	3 (10)

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison

of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other taliglucerase alfa products may be misleading.

Anti-Drug Antibodies (ADA)
In a clinical trial of treatment-naïve adults, 17 (53%) of 32 patients developed ADA during treatment with ELELYSO, and 2 (6%) of 32 patients tested positive for ADA at baseline prior to ELELYSO treatment. Of the 17 patients who developed ADA during ELELYSO treatment, 6 patients (35%) developed hypersensitivity reactions, 2 of whom met criteria for anaphylaxis. Two of the 17 patients who developed ADA during ELELYSO treatment discontinued treatment due to hypersensitivity reactions, one of whom had met criteria for anaphylaxis. Of the 2 patients who tested positive for ADA prior to initiation of ELELYSO treatment, one patient developed a hypersensitivity reaction during the first dose of ELELYSO and withdrew from the study. The second patient did not experience a hypersensitivity reaction.

In a clinical trial of treatment-naïve pediatric patients, 2 (22%) of 9 patients developed ADA during treatment with ELELYSO, and one of 9 patients was ADA-positive prior to initiation of ELELYSO. Two of these 3 patients experienced hypersensitivity reactions (1 who developed ADA during treatment and became negative after Week 12 and 1 who was ADA-positive at baseline and became ADA negative after Week 8) and continued treatment with ELELYSO. The third patient who developed ADA during treatment and continued to be ADA-positive until study completion at Week 52 did not experience a hypersensitivity reaction.

In clinical trials of 31 patients (26 adult and 5 pediatric patients) who switched from imiglucerase to ELELYSO treatment, 5 adults (16% of patients) developed ADA during treatment with ELELYSO. Four additional patients (13%, 2 adults and 2 children) tested positive for ADA at baseline but became ADA-negative after the switch to ELELYSO; one of these adult patients subsequently developed ADA to ELELYSO. Two adult patients (1 patient who developed ADA after the switch and 1 who was ADA positive at baseline) experienced hypersensitivity reactions. Both patients continued treatment with ELELYSO.

The relationship between ADA and hypersensitivity reactions is not fully understood. Monitoring for ADA to ELELYSO may be useful in ADA positive patients or in patients who have experienced hypersensitivity reactions to ELELYSO or other enzyme replacement therapies.

Neutralizing Antibodies
Thirty (30) of the 31 adult and pediatric patients who developed ADA to ELELYSO during treatment or tested positive for ADA at baseline were evaluated for neutralizing activity of the ADA in the mannose receptor binding and enzyme activity assays. Nineteen (63%) of the 30 patients had neutralizing antibodies capable of inhibiting mannose receptor binding of ELELYSO. Eight of these 19 patients had neutralizing antibodies capable of inhibiting the enzymatic activity of ELELYSO. Available data do not indicate a clear relationship between the presence of mannose receptor binding neutralizing antibodies or neutralizing antibodies capable of inhibiting the enzymatic activity of ELELYSO and the therapeutic response to ELELYSO.

Other Antibodies
Nine (29%) of the 31 adult and pediatric patients who developed ADA to ELELYSO during treatment or tested positive for ADA at baseline also developed antibodies against plant-specific glycans in ELELYSO.

6.3 Postmarketing Experience
The following adverse reactions have been identified during post-approval use of ELELYSO. Because these reactions include those reported voluntarily from a population of uncertain size in addition to those from postmarketing studies, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure:

- *Gastrointestinal disorders*: Vomiting, diarrhea
- *General disorders and administration site conditions*: Fatigue
- *Immune system disorders*: Anaphylaxis *[see Warnings and Precautions (5.1)]*, Type III immune-mediated fixed drug eruption
- *Musculoskeletal and connective tissue disorders*: Back pain

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

The limited available data on ELELYSO use in pregnant women are not sufficient to inform a drug-associated risk. However, there are clinical considerations *(see Clinical Considerations)*. In animal reproduction studies when pregnant rats and rabbits were administered taliglucerase alfa at intravenous doses up to 5 times the recommended human dose (RHD), there was no evidence of embryo-fetal toxicity *(see Data)*. The estimated background risk of major birth defects and miscarriage for the indicated population(s) are unknown. 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

Women with Type 1 Gaucher disease have an increased risk of spontaneous abortion if disease symptoms are not treated and controlled pre-conception and during a pregnancy. Pregnancy may exacerbate existing Type 1 Gaucher disease symptoms or result in new disease manifestations. Type 1 Gaucher disease manifestations may lead to adverse pregnancy outcomes, including hepatosplenomegaly which can interfere with the normal growth of a fetus and thrombocytopenia which can lead to increased bleeding and possible postpartum hemorrhage requiring transfusion.

Data

Animal Data

Reproduction studies have been performed with taliglucerase alfa administered during the period of organogenesis in rats and rabbits. In rats, intravenous doses up to 55 mg/kg/day (about 5 times the RHD of 60 units/kg based on the body surface area) did not cause any adverse effects on embryo-fetal development. In rabbits, intravenous doses up to 27.8 mg/kg/day (about 5 times the RHD of 60 units/kg based on the body surface area) did not show any embryo-fetal toxicity.

8.2 Lactation

Risk Summary

There are no data on the presence of taliglucerase alfa in human milk, the effects on the breast fed infant or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ELELYSO and any potential adverse effects on the breastfed child from ELELYSO or from the underlying maternal condition.

8.4 Pediatric Use

The use of ELELYSO for treatment of pediatric patients with Type 1 Gaucher disease 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 *[see Clinical Studies (14.1, 14.2), Clinical Pharmacology (12.3)]*. Data from 14 pediatric patients were included in the safety evaluation *[see Adverse Reactions (6.1)]*. There are insufficient data to inform dosing 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 *[see Adverse Reactions (6.1)]*.

8.5 Geriatric Use

During clinical trials, 8 patients aged 65 or older were treated with ELELYSO. Clinical trials of ELELYSO did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

11 DESCRIPTION

Taliglucerase alfa is a hydrolytic lysosomal glucocerebroside-specific enzyme produced by recombinant DNA technology using plant cell culture (carrot). Taliglucerase alfa is a monomeric glycoprotein enzyme containing 4 N-linked glycosylation sites (kDa=60.8). Taliglucerase alfa differs from native human glucocerebrosidase by two amino acids at the N terminal and up to 7 amino acids at the C terminal. Taliglucerase alfa is a glycosylated protein

with oligosaccharide chains at the glycosylation sites having terminal mannose sugars. These mannose-terminated oligosaccharide chains of taliglucerase alfa are specifically recognized by endocytic carbohydrate receptors on macrophages, the cells that accumulate lipid in Gaucher disease.

A unit is the amount of enzyme that catalyzes the hydrolysis of 1 micromole of the synthetic substrate para-nitrophenyl-β-D-glucopyranoside (*p*NP-Glc) per minute at 37 °C.

ELELYSO (taliglucerase alfa) for injection is supplied as a sterile, preservative-free, lyophilized powder for reconstitution and dilution prior to intravenous infusion. Each single-dose vial contains 200 units of taliglucerase alfa and D-mannitol (206.7 mg), polysorbate 80 (0.56 mg), and sodium citrate (30.4 mg). Citric acid may be added to adjust the pH at the time of manufacture. After reconstitution with 5.1 mL Sterile Water for Injection, USP, taliglucerase alfa concentration is 40 units/mL *[see Dosage and Administration (2)]*. Reconstituted solutions have a pH of approximately 6.0.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Gaucher disease is an autosomal recessive disorder caused by mutations in the human glucocerebrosidase gene, which results in a reduced activity of the lysosomal enzyme glucocerebrosidase. Glucocerebrosidase catalyzes the conversion of the sphingolipid glucocerebroside into glucose and ceramide. The enzymatic deficiency results in accumulation of substrate glucocerebroside primarily in the lysosomal compartment of macrophages, giving rise to foam cells or "Gaucher cells," which accumulate in the liver, spleen and bone marrow.

ELELYSO, a long term enzyme replacement therapy, is a recombinant analog of human lysosomal glucocerebrosidase that catalyzes the hydrolysis of glucocerebroside to glucose and ceramide, reducing the amount of accumulated glucocerebroside. ELELYSO uptake into cellular lysosomes is mediated by binding of ELELYSO mannose oligosaccharide chains to specific mannose receptors on the cell surface leading to internalization and subsequent transport to the lysosomes.

12.3 Pharmacokinetics

Pharmacokinetics of taliglucerase alfa were evaluated in 38 patients (29 adult and 9 pediatric patients) who received intravenous infusions of ELELYSO 30 units/kg or 60 units/kg every other week. ELELYSO 30 units/kg is not a recommended dose in treatment-naïve Gaucher disease patients *[see Dosage and Administration (2.1)]*. The pharmacokinetic parameters in adult and pediatric patients are summarized in Table 3.

In adult Type 1 Gaucher disease patients treated with ELELYSO 30 units/kg or 60 units/kg (N=29) every other week as initial therapy, pharmacokinetics were determined with the first dose and at Week 38 of treatment. The pharmacokinetics of taliglucerase alfa appeared to be nonlinear with a greater than dose-proportional increase in exposure at the doses studied.

No significant accumulation or change in taliglucerase alfa pharmacokinetics over time from Weeks 1 to 38 was observed with repeated dosages of 30 units/kg or 60 units/kg every other week. Based on the limited data, there were no significant pharmacokinetic differences between male and female patients in this study.

The pharmacokinetics of taliglucerase alfa were evaluated in 9 pediatric patients 4 to 17 years of age with Type 1 Gaucher disease who were treated with ELELYSO for 10 to 27 months. Six of the 9 patients were treatment-naïve, and 3 patients were switched from imiglucerase. In both the 30 units/kg and 60 units/kg dose groups, clearance values in pediatric patients were similar to those in adult patients. AUC values in pediatric patients were lower than AUC values in adult patients, due to weight-based dosing of taliglucerase alfa and lower body weights in pediatric patients.

Table 3: Taliglucerase Alfa Pharmacokinetic Parameters after Repeated Dosing in Adult and Pediatric Patients with Type 1 Gaucher Disease

	Pediatric Patients (N=9) Median (Range)		**Adult Patients at Week 38 (N=29) Median (Range)**	
	30 units/kg n = 5	**60 units/kg n = 4**	**30 units/kg n = 14**	**60 units/kg n = 15**
Age (years)	15 (10, 17)	11 (4, 16)	35 (19, 74)	33 (19, 58)

Weight (kg)	44.3 (22.8, 71.0)	28.6 (16.5, 50.4)	72.5 (51.5, 99.5)	73.5 (58.5, 87.0)[a]
$AUC_{0-\infty}$ (ng*h/mL)[b]	1416 (535, 1969)	2984 (1606, 4273)	2007 (1007, 10092)	6459 (2548, 21020)[a]
$T_{1/2}$ (min)	37.1 (22.5, 56.8)	32.5 (18.0, 42.9)	18.9 (9.20, 57.9)	28.7 (11.3, 104)[a]
CL (L/h)	30.5 (17.4, 37.8)	15.8 (11.7, 24.9)	30.5 (6.79, 68.0)	18.5 (6.20, 37.9)[a]
V_{ss} (L)	14.9 (10.1, 35.6)	8.80 (3.75, 21.4)	11.7 (2.3, 22.7)	10.7 (1.4, 18.5)[a]

[a] n = 14
[b] Values were derived from concentration data expressed in ng/mL

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential or studies to evaluate mutagenic potential have not been performed with taliglucerase alfa. In a male and female fertility study in rats, taliglucerase alfa did not cause any significant adverse effect on male or female fertility parameters up to a maximum dose of 55 mg/kg/day (about 5 times the recommended human dose of 60 units/kg based on the body surface area).

14 CLINICAL STUDIES

14.1 Clinical Trials of ELELYSO as Initial Therapy

Clinical Trial in Patients 19 Years and Older

The safety and efficacy of ELELYSO were assessed in 31 adult patients with Type 1 Gaucher disease. The trial was a 9-month, multi-center, double-blind, randomized trial in 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. Patients were 19 to 74 years of age (mean age 36 years), and 48% were male. Patients were randomized to receive ELELYSO at a dosage of either 30 units/kg (n=15) or 60 units/kg (n=16) every other week. The recommended 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 *[see Dosage and Administration (2.1)]*.

Table 4 shows the baseline values and mean (SD) changes in clinical parameters (spleen volume, liver volume, platelet count, and hemoglobin) after 9 months of treatment with ELELYSO. For all clinical trials, liver and spleen volumes were measured by MRI and are reported as percentage of body weight (%BW) and multiples of normal (MN). The observed change from baseline in the primary endpoint, reduction in spleen volume, was considered to be clinically meaningful in light of the natural history of untreated Gaucher disease.

Table 4: Mean (SD) Changes in Clinical Parameters from Baseline to 9 Months in Treatment-Naïve Adults with Type 1 Gaucher Disease Initiating Therapy with ELELYSO (N=31)**

	Clinical Parameter	30 units/kg* (n=15) Mean (SD)	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)

*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. *[see Dosage and Administration (2.1)]*
** *SD = standard deviation*
♮ *%BW = percentage of body weight*
♯ *MN = multiples of normal*

Twenty-six of the 31 patients in this 9-month clinical trial continued blinded treatment with ELELYSO in an extension trial for a total treatment duration of 24 months. The following data are the changes in clinical parameters from baseline to Month 24 for the 30 units/kg (n=12) and 60 units/kg (n=14) dose 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. Twenty-three of the 26 patients who continued open-label treatment with ELELYSO for additional 12 months demonstrated stability in these clinical parameters.

Clinical Trial in Patients 16 years and Younger
The safety and efficacy of ELELYSO were assessed in 9 pediatric patients with Type 1 Gaucher disease. The trial was a 12-month, multi-center, double-blind, randomized study in treatment-naïve patients. Patients were 2 to 13 years of age (mean age 8.1 years), and 67% were male. Patients were randomized to receive ELELYSO at a dosage of either 30 units/kg (n=4) or 60 units/kg (n=5) every other week. The recommended ELELYSO dosage in treatment-naïve pediatric patients is 60 units/kg every other week. ELELYSO 30 units/kg every other week is not a recommended dosage *[see Dosage and Administration (2.1)]*.

The following data 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.

Nine pediatric patients in the 12-month clinical trial continued blinded treatment with ELELYSO in an extension trial for a total treatment duration of 24 months. The following data are the changes [median (Q1, Q3)] in clinical parameters from baseline to Month 24 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.

14.2 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. The trial was a 9-month, multi-center, open-label, single arm study in patients who had been receiving 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 dose of imiglucerase for at least 6 months prior to enrollment. Patients were 6 to 66 years of age (mean age 42 years, including pediatric patients), and 55% were male. 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. 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).

Mean (SD) organ volumes and hematologic values remained stable through 9 months of ELELYSO treatment. 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. 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. ELELYSO dose 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.

Eighteen of the 26 adult patients who completed the 9-month clinical trial continued treatment with ELELYSO in an open-label extension trial for additional 27 months (total treatment 36 months). 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.

Five pediatric patients in the 9-month clinical trial who continued open-label treatment with ELELYSO for additional 24 months demonstrated stability in these clinical parameters.

16 HOW SUPPLIED/STORAGE AND HANDLING

ELELYSO (taliglucerase alfa) for injection is supplied as a sterile, preservative-free, white to off-white lyophilized powder in a single-dose vial. Each vial of ELELYSO contains 200 units of taliglucerase alfa.

Each carton contains one vial (NDC 0069-0106-01).

Store ELELYSO refrigerated at 2 °C to 8 °C (36 °F to 46 °F) in the original carton to protect from light. Do not freeze.

17 PATIENT COUNSELING INFORMATION

Hypersensitivity Reactions Including Anaphylaxis

Advise patients and caregivers that reactions related to administration and infusion may occur during and after ELELYSO treatment, including life-threatening anaphylaxis and severe hypersensitivity reactions. Inform patients of the signs and symptoms of anaphylaxis and hypersensitivity reactions, and have them seek medical care should signs and symptoms occur. Inform patients that they should be carefully re-evaluated for treatment with ELELYSO if serious hypersensitivity reactions, including anaphylaxis, occur. Reduction of the infusion rate and/or pre-treatment with antihistamines, antipyretics and/or corticosteroids may prevent subsequent reactions *[see Warnings and Precautions (5.1)]*.

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