Current Therapies and Research for Type 1 Gaucher Disease

An Interview with Gregory A. Grabowski, MD

Effect of Long-Term Treatment for Type 1 Gaucher Disease

New Study Finds That Patients Show Significant Improvement After 10 Years of Enzyme Replacement Therapy

Patient Profile: Herman Platt

Ask the Case Manager

Cerezyme.com Mapped!
As researchers learn more about type 1 Gaucher disease, treatments continue to evolve. This issue of Horizons features two articles about advances in our knowledge about the disease: On page 3, we feature an interview with Gregory A. Grabowski, MD, professor and director at Cincinnati Children’s Hospital Medical Center in Ohio, discussing “Gaucher disease and other storage disorders,” an article he recently published.

On page 5, we speak with Neal Weinreb, MD, of Northwest Oncology Hematology Associates in Coral Springs, Florida, about a new study on the effect of long-term treatment for type 1 Gaucher disease. Dr. Weinreb was lead author of the study, which found that patients show significant improvement after 10 years of enzyme replacement therapy.

This issue also features the premier of the new “Ask the Case Manager” series, on page 11. In this series, Genzyme Case Managers answer common questions that patients with type 1 Gaucher disease and their families often ask. We encourage you to send us your questions for future columns by filling out the postcard in the centerfold of this issue of Horizons.

Finally, on page 12, Herman Platt offers an interesting and energetic patient profile, and on page 14 you’ll find a complete guide to Cerezyme.com.

Your feedback and comments are always welcome. Help shape your own Horizons by letting us hear from you.

—Your team at Genzyme

Cerezyme® (imiglucerase for injection) is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of type 1 Gaucher disease that results in one or more of the following conditions: anemia (low red blood cell count), thrombocytopenia (low blood platelet count), bone disease, hepatomegaly or splenomegaly (enlarged liver or spleen).

Important Safety Information
Approximately 15% of patients have developed immune responses (antibodies). These patients have a higher risk of an allergic reaction (hypersensitivity). Use Cerezyme® (imiglucerase for injection) carefully if you have had an allergic reaction to the product in the past. Symptoms suggestive of allergic reaction happen in 6.6% of patients, and include anaphylactoid reaction (a serious allergic reaction), itching, flushing, hives, an accumulation of fluid under the skin, chest discomfort, shortness of breath, coughing, cyanosis (a bluish discoloration of the skin due to diminished oxygen), and low blood pressure. Side effects related to Cerezyme administration have been reported in less than 15% of patients. Each of the following events occurred in less than 2% of the total patient population. Reported side effects include nausea, abdominal pain, vomiting, diarrhea, rash, fatigue, headache, fever, dizziness, chills, backache, and rapid heart rate. Because Cerezyme therapy is administered by intravenous infusion, reactions at the site of injection may occur: discomfort, itching, burning, swelling or uninfected abscess. Cerezyme is available by prescription only. For more information, consult your physician.

Please see accompanying full Prescribing Information on pages 9-10.

Patients are encouraged to report negative side effects of prescription drugs to the FDA. Visit FDA.gov/medwatch, or call 1-800-FDA-1088.
Current Therapies and Research for Type 1 Gaucher Disease

An Interview with Gregory A. Grabowski, MD

As researchers learn more about type 1 Gaucher disease, treatments continue to evolve. Gregory A. Grabowski, MD, professor and director at Cincinnati Children’s Hospital Medical Center in Ohio, recently published an article, “Gaucher disease and other storage disorders,” in the journal Hematology. Horizons interviewed Dr. Grabowski about topics including this article and therapies and research for type 1 Gaucher disease.

When was Gaucher disease first discovered?
Type 1 Gaucher disease was first described in 1882 by Dr. Philippe Gaucher in Paris as his thesis for his medical degree. His patient was a 32-year-old female with a massively enlarged spleen. Dr. Gaucher later concluded that she died of a new type of tumor of the spleen. It wasn’t until the 1890s that more patients would be examined and described, and when Dr. William Osler would name the disease Gaucher disease. In the early 1900s, Gaucher disease was recognized as a disease that affected the whole body, and that ran in families.

How common are lysosomal storage disorders (LSDs) such as Gaucher disease?
The LSDs are a group of about 50 different diseases that together occur in about 1 in 7000 live births. The frequencies of these diseases vary with the disease type, but Gaucher, Fabry, and Pompe disease appear to be the most common LSDs. There are several different types of each of these disorders, and Gaucher disease has been clinically divided into three types: 1, 2, and 3.

Type 1 Gaucher disease is a non-neuronopathic disease, which means that it involves most organs and tissues, but not usually the brain. Types 2 and 3 are neuronopathic and directly involve the brain.

Type 1 Gaucher disease has its greatest incidence in the Ashkenazi Jewish population, in which it occurs in about 1 in every 800 to 1 in every 1000 Ashkenazi Jews. In the non-Ashkenazi population, the incidence ranges from 1 in every 50,000 to 1 in every 80,000 individuals.

What effects does type 1 Gaucher disease have on organs in the body?
Type 1 Gaucher disease involves most of the organs other than the brain. The major organs of clinical concern in all patients with this disease are the spleen, liver, and the bone and bone marrow. The lungs and other systems are involved less often. The liver can become enlarged, and the spleen and bone marrow involvement can cause low platelet counts and anemia. Approximately 30% to 40% of children with untreated type 1 Gaucher disease experience delayed growth, having lower than normal height and weight during childhood.

In addition to bone marrow (the inside of bone), the supporting bone structure is changed in many patients, with lower calcium content, reduced bone mass (osteopenia), or severe bone loss (osteoporosis). An abnormality called avascular necrosis (AVN) results from an area of bone being deprived of its normal blood supply. This can be found in many patients, and often occurs with few or no pain symptoms. In about 10% of patients, bone pain, or “bone crisis,” occurs and leads to difficulties. These are detected by magnetic resonance imaging (MRI) and/or x-ray scans several weeks to months after they have occurred.

Can you briefly explain the gene mutations that cause type 1 Gaucher disease?
There are over 350 different changes or mutations in the Gaucher disease gene, GBA1, that cause the disease. These mutations result from a change in the DNA of the gene. The gene is composed of a string of chemicals called nucleic acids. Only some of these contain the genetic information needed to make the Gaucher disease enzyme, glucocerebrosidase.

Most of the 350 mutations in GBA1 that cause Gaucher disease result from a change in only one of the nucleic acids. This change leads to the production of an abnormally functioning enzyme that cannot “digest” the Gaucher disease lipid, called glucocerebroside.

Does enzyme replacement therapy, which is used to treat Gaucher disease, target specific tissues in the body?
In Gaucher disease, enzyme replacement therapy needs to be directed to cells called macrophages. On the surface of the macrophage there is a protein, called a receptor, that recognizes specific types of sugars. For Gaucher disease enzyme replacement therapy, the mannose receptor is the most important. So glucocerebrosidases that have mannose on them attach to the mannose receptor and are delivered into the macrophage lysosomes, where they are needed to digest the excess glucocerebroside.

One way to think about it is that the enzyme replacement therapy uses the receptors to deliver the enzymes to the correct cells for treatment—sort of like how the postal service uses zip codes to directly deliver the mail!
What drugs are currently approved for treating type 1 Gaucher disease?
Currently, three enzyme replacement drugs are approved by the U.S. Food and Drug Administration (FDA) to treat type 1 Gaucher disease: Cerezyme® (imiglucerase for injection; see Important Safety Information, page 2, and Product Information, centerfold), VPRIV® (velaglucerase alfa), and Elelyso® (taliglucerase alfa). Some of these medications are restricted to certain age groups.

Zavesca® (miglustat) is FDA-approved as a secondary drug for those individuals with type 1 Gaucher disease who cannot receive enzyme replacement therapy for various medical reasons. This drug is not enzyme replacement therapy. Instead, it decreases the body’s ability to make glucocerebroside. The patient’s own enzyme can then digest a lower amount of the lipid coming into the cells. This type of treatment is called *substrate reduction therapy*.

Is bone marrow or stem-cell transplantation useful for type 1 Gaucher disease?
Bone marrow transplantation (BMT) or hematopoietic stem-cell transplantation (HSCT) has been used for some people with type 1 Gaucher disease. This can improve an enlarged liver and correct anemia and low platelet counts. Not much information is known about how bone may be involved.

BMT and HSCT are not recommended for type 1 Gaucher disease.

How are the Gaucher disease registries beneficial for research/development of new treatments?
The International Collaborative Gaucher Group (ICGG) Gaucher Registry (of more than 6000 patients with Gaucher disease) and other registries are very valuable for learning more about Gaucher disease and its treatments. I am most familiar with the data in the ICGG Registry, and the patient outcome data on treated (approximately 5000) and untreated (approximately 1000) patients has resulted in over 30 publications about the effects of Gaucher disease and its therapies.

Because of this, the ICGG Registry has been the major source of new and important information for understanding the difficulties and issues in type 1 Gaucher disease for the past 20 years. These data provide new insights that help physicians improve the care and health of their patients.

Are research developments in other neurodegenerative diseases such as Parkinson’s disease or Alzheimer’s disease related to possible treatments for type 1 Gaucher disease?
Actually, the reverse is happening. Gaucher disease treatments are having or will have a significant impact on the development of treatments for Parkinson’s and Alzheimer’s disease. Data now strongly support the idea that mutations in the *GBA1* gene may also be involved in Parkinson’s disease. So, persons who are diagnosed with Parkinson’s disease who carry a *GBA1* mutation have earlier onset and more progressive disease. Researchers are beginning to understand more about the effects of the *GBA1* mutation on the basic Parkinson’s disease processes, which may lead to improved treatments for the disease.

Importantly, the “risk” of a Gaucher disease carrier developing Parkinson’s disease is not known, but it is likely to be low.

Do you think clinical trials seem promising for discovering new therapies for type 1 Gaucher disease?
Currently, therapy with eliglustat is being tested on patients in clinical trials, and more data should become available in the next 6 to 12 months.

Other approaches are in the very early stages of development, including substrate reduction therapies that could affect the brain involvement in types 2 and 3 Gaucher disease. *Chaperone therapies* (potential oral drugs) and several other cell-based and/or gene therapy approaches are being investigated. This is a very active area of basic and preclinical research.
Effect of Long-Term Treatment for Type 1 Gaucher Disease

New Study Finds That Patients Show Significant Improvement After 10 Years of Enzyme Replacement Therapy

The first enzyme replacement therapy to treat type 1 Gaucher disease was alglucerase in 1991, followed by imiglucerase in 1994. “When enzyme replacement therapy for Gaucher disease was first approved in 1991, the concept was revolutionary and untested in more than a handful of patients,” said Neal Weinreb, MD, lead author of the study.

Dr. Weinreb, of Northwest Oncology Hematology Associates in Coral Springs, Florida, and co-investigators in the International Collaborative Gaucher Group (ICGG) sought to determine the effects of long-term Ceredase/Cerezyme treatment. Previous studies had looked at treatment effects after approximately 5 years of treatment, but they wanted to learn about patients’ responses after 10 years of treatment.

Using Valuable Patient Data from the Gaucher Registry

For this study, Dr. Weinreb’s group used data from patients who consented to be included in the ICGG Gaucher Registry. The Gaucher Registry, sponsored by Genzyme, a Sanofi Company, but governed by independent scientific advisors, is a unique resource, with a current enrollment of more than 6000 patients worldwide.

“The 757 patients who were included in this study constitute about one-third of all Registry patients in whom treatment was begun prior to 1999. This large number of patients is geographically and ethnically representative of the type 1 Gaucher disease population worldwide, and therefore an accurate snapshot of real-life experience,” Dr. Weinreb said.

For some of these patients, the Registry already has more than 20 years of information. “Because the data is already in hand, we can generate answers now or in the near future that might otherwise be unavailable for many years,” he said.

The Study of 10 Years of Enzyme Replacement Therapy

In October 2011, Dr. Weinreb and colleagues looked at data from patients with type 1 Gaucher disease at “baseline,” which was 12 months before treatment to one month after the start of treatment. They compared this to patient data after 10 years of enzyme replacement therapy.

Many of the patients included in this study had been diagnosed with type 1 Gaucher disease early in life, with the average age at diagnosis being 11 years old. The average age for starting Cerezyme treatment was 24 years. Nowadays, in most developed nations, it is unusual for young symptomatic patients to have to wait so long from diagnosis to treatment, but 15 to 20 years ago, enzyme replacement therapy was much less accessible.

A total of 757 patient cases were included in the study. Of these, 226 patients had received only Cerezyme and 531 patients had started on Ceredase and were then switched to Cerezyme when it became available.

Individuals in the study were categorized by whether they had had their spleens removed (splenectomized) or not. The study examined the data on 200 patients who had had splenectomies and 557 who had not. Spleen removal has an impact on the progression of the disease, and can also influence the body’s response to treatments.

Investigators noted that at the time of the first infusion, the patients with splenectomies had a lower incidence of anemia (low red blood cell count) and thrombocytopenia (low platelet count). Liver enlargement occurred similarly in the two groups. Patients with splenectomies were more likely to have bone pain and “bone crisis” (sudden loss of blood supply in the bone, which causes severe pain and localized bone death).

The investigators analyzed the following characteristics of patients prior to the start of therapy, and then at 10 years after therapy with Ceredase/Cerezyme:

- Hemoglobin
- Platelet count
- Liver volume
- Spleen volume
- Bone pain
- Bone crisis

“It is important to note that in this study, we examined only blood, spleen, and liver responses, as well as changes in bone pain. We did not study other important outcomes such as changes in bone density or occurrence of fractures or some other severe bone conditions. Ten years is also too short a time frame in which to investigate other important outcomes such as Parkinson disease or occurrence of malignancies,” said Dr. Weinreb.
### Study Results: Improvements in Patients After 10 Years of Ceredase/Cerezyme Treatment

<table>
<thead>
<tr>
<th></th>
<th>Splenectomized Patients</th>
<th>Non-Splenectomized Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anemia</strong></td>
<td>95% not anemic compared to 74% before treatment</td>
<td>93% not anemic compared to 57% before treatment</td>
</tr>
<tr>
<td><strong>Low platelet count</strong></td>
<td>99% in normal-to-mild range compared to 86% before treatment</td>
<td>77% in normal-to-mild range compared to 24% before treatment</td>
</tr>
<tr>
<td><strong>Enlarged spleen</strong></td>
<td>Not applicable</td>
<td>56% who were moderate-to-severe now in normal-to-mild range; only 1 patient (1%) remained with severe splenomegaly</td>
</tr>
<tr>
<td><strong>Enlarged liver</strong></td>
<td>81% now in normal-to-mild range compared to 19% before treatment</td>
<td>86% now in normal-to-mild range compared to 20% before treatment</td>
</tr>
<tr>
<td><strong>Bone pain</strong></td>
<td>39% had no bone pain compared to 11% before treatment</td>
<td>70% had no bone pain compared to 48% before treatment</td>
</tr>
<tr>
<td><strong>Severe bone pain (bone crisis)</strong></td>
<td>Only 3 patients (6%) still had bone crises compared to 38% before treatment</td>
<td>Only 2 patients (1%) still had bone crises compared to 16% before treatment</td>
</tr>
</tbody>
</table>

### Encouraging Results of the Study

The study found that after 10 years of treatment with Ceredase/Cerezyme, responses that had been achieved earlier in the treatment course were maintained: Compared to pretreatment status, there was a significant improvement in hemoglobin concentration, platelet count, liver size, and spleen size. The treatment also resulted in significantly improved skeletal symptoms, with decreased bone pain and virtual absence of bone crises in patients with and without splenectomies. However, because patients with splenectomies were much more likely to have chronic bone pain before the start of treatment due to pre-existing irreversible bone complications, proportionately fewer splenectomized patients were free of bone pain after 10 years, compared with patients whose spleens had not been removed. (See chart on “Study Results: Improvements in Patients After 10 Years of Ceredase/Cerezyme Treatment.”)

“Our study demonstrates that with long-term Cerezyme treatment, most patients will achieve and maintain normal or near-normal blood counts and liver size,” Dr. Weinreb said. “Although many patients will still have some minor enlargement of the spleen, practically none should have continued abdominal discomfort or eating problems. For patients free of irreversible bone damage prior to starting enzyme replacement therapy, long-term Cerezyme should be helpful in preventing or helping treat Gaucher disease-associated bone pain.”

“Our observations...will provide useful guidance for physicians who are managing patients who may have questions about the value of long-term treatment with Cerezyme,” said Dr. Weinreb.

### The Importance of Staying on Enzyme Therapy

Dr. Weinreb emphasized the importance of patients continuing enzyme replacement therapy. “Patients can be reassured that continued enzyme replacement therapy is highly effective in maintaining initial gains, and that there is no evidence for development of resistance to treatment, even after 10 years.”

As for future studies, Dr. Weinreb said, “We anticipate that future Gaucher Registry studies will extend that time frame to 20 years or more.”

### Indications and Usage

Cerezyme® (imiglucerase for injection) is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of type 1 Gaucher disease that results in one or more of the following conditions: anemia (low red blood cell count), thrombocytopenia (low blood platelet count), bone disease, hepatomegaly or splenomegaly (enlarged liver or spleen).

### Important Safety Information

Approximately 15% of patients have developed immune responses (antibodies). These patients have a higher risk of an allergic reaction (hypersensitivity). Use Cerezyme® (imiglucerase for injection) carefully if you have had an allergic reaction to the product in the past. Symptoms suggestive of allergic reaction happen in 6.6% of patients, and include anaphylactoid reaction (a serious allergic reaction), itching, flushing, hives, an accumulation of fluid under the skin, chest discomfort, shortness of breath, coughing, cyanosis (a bluish discoloration of the skin due to diminished oxygen), and low blood pressure. Side effects related to Cerezyme administration have been reported in less than 15% of patients. Each of the following events occurred in less than 2% of the total patient population. Reported side effects include nausea, abdominal pain, vomiting, diarrhea, rash, fatigue, headache, fever, dizziness, chills, backache, and rapid heart rate. Because Cerezyme therapy is administered by intravenous infusion, reactions at the site of injection may occur: discomfort, itching, burning, swelling or uninfected abscess. Cerezyme is available by prescription only. For more information, consult your physician. To learn more, please see the enclosed full product information or contact Genzyme at 1-800-745-4447 (option 2).

Please see accompanying full Prescribing Information on pages 9-10.
Would you be interested in sharing your story of living with Gaucher disease? If so, please fill in the following:

Name ____________________________________________
Address __________________________________________
City __________________________ State __________ Zip __________
Email ____________________________________________
Phone ____________________________________________

Send us your questions for our new “Ask the Case Manager” column!

What questions would you like to see answered in an upcoming issue of *Horizons*:

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

If you have enjoyed this issue of *Horizons*, please let us know by completing and returning the postage-paid Business Reply Card below.
**DESCRIPTION**

Cerezyme® (imiglucerase for injection) is an analogue of the human enzyme β-glucocerebrosidase, produced by recombinant DNA technology. β-Glucocerebrosidase (β-D-glucosyl-N-acylsphingosine glucohydrolase, E.C. 3.2.1.45) is a lysosomal glycoprotein enzyme which catalyzes the hydrolysis of the glycolipid glucocerebroside to glucose and ceramide.

Cerezyme® is 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 different from those on placental glucocerebrosidase. These mannose-terminated oligosaccharide chains of imiglucerase are specifically recognized by endocytic carbohydrate receptors on macrophages, the cells that accumulate lipid in Gaucher disease.

Cerezyme® is supplied as a sterile, non-pyrogenic, white to off-white lyophilized product. The quantitative composition of the lyophilized drug is provided in the following table:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>200 Unit Vial</th>
<th>400 Unit Vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imiglucerase (total amount)*</td>
<td>212 units</td>
<td>424 units</td>
</tr>
<tr>
<td>Mannitol</td>
<td>170 mg</td>
<td>340 mg</td>
</tr>
<tr>
<td>Sodium Citrates</td>
<td>70 mg</td>
<td>140 mg</td>
</tr>
<tr>
<td>(Trisodium Citrate)</td>
<td>(52 mg)</td>
<td>(104 mg)</td>
</tr>
<tr>
<td>(Disodium Hydrogen Citrate)</td>
<td>(18 mg)</td>
<td>(36 mg)</td>
</tr>
<tr>
<td>Polysorbate 80, NF</td>
<td>0.53 mg</td>
<td>1.06 mg</td>
</tr>
<tr>
<td>Citric Acid and/or Sodium Hydroxide may have been added at the time of manufacture to adjust pH.</td>
<td></td>
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</tr>
</tbody>
</table>

*This provides a respective withdrawal dose of 200 and 400 units of imiglucerase.

An enzyme unit (U) is defined as the amount of enzyme that catalyzes the hydrolysis of 1 micromole of the synthetic substrate para-nitrophenyl-β-D-glucopyranoside (pNP-Glc) per minute at 37°C. The product is stored at 2-8°C (36-46°F). After reconstitution with Sterile Water for Injection, USP, the imiglucerase concentration is 40 U/mL (see DOSAGE AND ADMINISTRATION for final concentrations and volumes). Reconstituted solutions have a pH of approximately 6.1.

**CLINICAL PHARMACOLOGY**

**Mechanism of Action/Pharmacodynamics**

Gaucher disease is characterized by a deficiency of β-glucocerebrosidase activity, resulting in accumulation of glucocerebroside in tissue macrophages which become engorged and are typically found in the liver, spleen, and bone marrow and occasionally in lung, kidney, and intestine. Secondary hematologic sequelae include severe anemia and thrombocytopenia in addition to the characteristic progressive hepatosplenomegaly, skeletal complications, including osteonecrosis and osteopenia with secondary pathological fractures. Cerezyme® (imiglucerase for injection) catalyzes the hydrolysis of glucocerebroside to glucose and ceramide. In clinical trials, Cerezyme improved anemia and thrombocytopenia, reduced spleen and liver size, and decreased cachexia to a degree similar to that observed with Ceredase® (algglucerase injection).

**Pharmacokinetics**

During one-hour intravenous infusions of four doses (7.5, 15, 30, 60 U/kg) of Cerezyme® (imiglucerase for injection), steady-state enzymatic activity was achieved by 30 minutes. Following infusion, plasma enzymatic activity declined rapidly with a half-life ranging from 3.6 to 10.4 minutes. Plasma clearance ranged from 9.8 to 20.3 mL/min/kg (mean ± S.D., 14.5 ± 4.0 mL/min/kg). The volume of distribution corrected for weight ranged from 0.09 to 0.15 L/kg (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. The pharmacokinetics of Cerezyme do not appear to be different from placental-derived alglucerase (Ceredase®).

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 WARNINGS).

**INDICATIONS AND USAGE**

Cerezyme® (imiglucerase for injection) is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of Type 1 Gaucher disease that results in one or more of the following conditions:

- a. anemia
- b. thrombocytopenia
- c. bone disease
- d. hepatomegaly or splenomegaly

**CONTRAINDICATIONS**

There are no known contraindications to the use of Cerezyme® (imiglucerase for injection). Treatment with Cerezyme should be carefully re-evaluated if there is significant clinical evidence of hypersensitivity to the product.

**WARNINGS**

Approximately 15% of patients treated and tested to date have developed IgG antibody to Cerezyme® (imiglucerase for injection) 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 a higher risk of hypersensitivity reaction. Conversely, not all patients with symptoms of hypersensitivity have detectable IgG antibody. It is suggested that patients be monitored periodically for IgG antibody formation during the first year of treatment.

Treatment with Cerezyme should be approached with caution in patients who have exhibited symptoms of hypersensitivity to the product.

Anaphylactoid reaction has been reported in less than 1% of the patient population. Further treatment with imiglucerase should be conducted with caution. Most patients have successfully continued therapy after a reduction in rate of infusion and pretreatment with antihistamines and/or corticosteroids.

**PRECAUTIONS**

**General**

In less than 1% of the patient population, pulmonary hypertension and pneumonia have also been observed during treatment with Cerezyme® (imiglucerase for injection). Pulmonary hypertension and pneumonia are known complications of Gaucher disease and have been observed both in patients receiving and not receiving Cerezyme. No causal relationship with Cerezyme has been established. Patients with respiratory symptoms in the absence of fever should be evaluated for the presence of pulmonary hypertension.

Therapy with Cerezyme should be directed by physicians knowledgeable in the management of patients with Gaucher disease.

Caution may be advisable in administration of Cerezyme to patients previously treated with Ceredase® (algglucerase injection) and who have developed antibody to Ceredase or who have exhibited symptoms of hypersensitivity to Ceredase.
Carcinogenesis, Mutagenesis, Impairment of Fertility
Studies have not been conducted in either animals or humans to assess the potential effects of Cerezyme® (imiglucerase for injection) on carcinogenesis, mutagenesis, or impairment of fertility.

Teratogenic Effects: Pregnancy Category C
Animal reproduction studies have not been conducted with Cerezyme® (imiglucerase for injection). It is also not known whether Cerezyme can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Cerezyme should not be administered during pregnancy except when the indication and need are clear and the potential benefit is judged by the physician to substantially justify the risk.

Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Cerezyme® (imiglucerase for injection) is administered to a nursing woman.

Pediatric Use
The safety and effectiveness of Cerezyme® (imiglucerase for injection) have been established in patients between 2 and 16 years of age. Use of Cerezyme in this age group is supported by evidence from adequate and well-controlled studies of Cerezyme and Ceredase® (algglucerase injection) in adults and pediatric patients, with additional data obtained from the medical literature and from long-term post-marketing experience. Cerezyme has been administered to patients younger than 2 years of age, however the safety and effectiveness in patients younger than 2 have not been established.

ADVERSE REACTIONS
Since the approval of Cerezyme® (imiglucerase for injection) in May 1994, Genzyme has maintained a worldwide post-marketing database of spontaneously reported adverse events and adverse events discussed in the medical literature. The percentage of events for each reported adverse reaction term has been calculated using the number of patients from these sources as the denominator for total patient exposure to Cerezyme since 1994. Actual patient exposure is difficult to obtain due to the voluntary nature of the database and the continuous accrual and loss of patients over that span of time. The actual number of patients exposed to Cerezyme since 1994 is likely to be greater than estimated from these voluntary sources and, therefore, the percentages calculated for the frequencies of adverse reactions are most likely greater than the actual incidences.

Experience in patients treated with Cerezyme has revealed that approximately 13.8% of patients experienced adverse events which were judged to be related to Cerezyme administration and which occurred with an increase in frequency. Some of the adverse events were related to the route of administration. These include discomfort, pruritus, burning, swelling or sterile abscess at the site of venipuncture. Each of these events was found to occur in < 1% of the total patient population.

Symptoms suggestive of hypersensitivity have been noted in approximately 6.6% of patients. Onset of such symptoms has occurred during or shortly after infusions; these symptoms include pruritus, flushing, urticaria, angioedema, chest discomfort, dyspnea, coughing, cyanosis, and hypotension. Anaphylactoid reaction has also been reported (see WARNINGS). Each of these events was found to occur in < 1.5% of the total patient population.

In addition to the adverse reactions that have been observed in patients treated with Cerezyme, transient peripheral edema has been reported for this therapeutic class of drug.

OVERDOSE
Experience with doses up to 240 U/kg every 2 weeks have been reported. At that dose there have been no reports of obvious toxicity.

DOSAGE AND ADMINISTRATION
Cerezyme® (imiglucerase for injection) is administered by intravenous infusion over 1-2 hours. Dosage should be individualized to each patient. Initial dosages range from 2.5 U/kg of body weight 3 times a week to 60 U/kg once every 2 weeks. 60 U/kg every 2 weeks is the dosage for which the most data are available. Disease severity may dictate that treatment be initiated at a relatively high dose or relatively frequent administration.

Dosage adjustments should be made on an individual basis and may increase or decrease, based on achievement of therapeutic goals as assessed by routine comprehensive evaluations of the patient’s clinical manifestations.

Cerezyme® should be stored at 2-8°C (36-46°F). After reconstitution, Cerezyme should be inspected visually before use. Because this is a protein solution, slight flocculation (described as thin translucent fibers) occurs occasionally after dilution. The diluted solution may be filtered through an in-line low protein-binding 0.2 μm filter during administration. Any vials exhibiting opaque particles or discoloration should not be used. DO NOT USE Cerezyme after the expiration date on the vial.

On the day of use, after the correct amount of Cerezyme to be administered to the patient has been determined, the appropriate number of vials are each reconstituted with Sterile Water for Injection, USP. The final concentrations and administration volumes are provided in the following table:

<table>
<thead>
<tr>
<th></th>
<th>200 Unit Vial</th>
<th>400 Unit Vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterile water for reconstitution</td>
<td>5.1 mL</td>
<td>10.2 mL</td>
</tr>
<tr>
<td>Final volume of reconstituted product</td>
<td>5.3 mL</td>
<td>10.6 mL</td>
</tr>
<tr>
<td>Concentration after reconstitution</td>
<td>40 U/mL</td>
<td>40 U/mL</td>
</tr>
<tr>
<td>Withdrawal volume</td>
<td>5.0 mL</td>
<td>10.0 mL</td>
</tr>
<tr>
<td>Units of enzyme within final volume</td>
<td>200 units</td>
<td>400 units</td>
</tr>
</tbody>
</table>

A nominal 5.0 mL for the 200 unit vial (10.0 mL for the 400 unit vial) is withdrawn from each vial. The appropriate amount of Cerezyme for each patient is diluted with 0.9% Sodium Chloride Injection, USP, to a final volume of 100 – 200 mL. Cerezyme is administered by intravenous infusion over 1-2 hours. Aseptic techniques should be used when diluting the dose. Since Cerezyme does not contain any preservative, after reconstitution, vials should be promptly diluted and not stored for subsequent use. Cerezyme, after reconstitution, has been shown to be stable for up to 12 hours when stored at room temperature (25°C) and at 2-8°C. Cerezyme, when diluted, has been shown to be stable for up to 24 hours when stored at 2-8°C.

Relatively low toxicity, combined with the extended time course of response, allows small dosage adjustments to be made occasionally to avoid discarding partially used bottles. Thus, the dosage administered in individual infusions may be slightly increased or decreased to utilize fully each vial as long as the monthly administered dosage remains substantially unaltered.

HOW SUPPLIED
Cerezyme® (imiglucerase for injection) is supplied as a sterile, non-pyrogenic, lyophilized product. It is available as follows:

200 Units per Vial NDC 58468-1983-1
400 Units per Vial NDC 58468-4663-1

Store at 2-8°C (36-46°F).

Rx only

Cerezyme® (imiglucerase for injection) is manufactured by:
Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142 USA

Certain manufacturing operations may have been performed by other firms.

Cerezyme and Genzyme are registered trademarks of Genzyme Corporation.

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In this new series, Genzyme Case Managers answer common questions that patients with type 1 Gaucher disease and their families often ask. We encourage you to send us your questions for future columns by filling out the postcard in the centerfold of this issue of Horizons.

This month, we spoke with two Genzyme Case Managers: Robert Tucker and Eileen Walsh.

Question: I am concerned about whether my insurance company will pay for my medication and whether I can afford my deductibles, co-payments, or co-insurance.

Answer, from Robert Tucker, Genzyme Case Manager:
I am often asked these types of questions by patients and their families. To answer the questions and ease their worries, I explain that as their Genzyme Case Manager, I am dedicated to ensuring they have access to their treatment. In most cases, insurance will pay for enzyme replacement therapy, but there are also organizations and resources, such as the Genzyme Co-Pay Assistance Program, that may be able to help with out-of-pocket expenses. If a patient lacks insurance entirely, we work together to apply for insurance, find assistance for premiums, and if necessary work through Genzyme’s Charitable Access Program to obtain medication.

Eileen Walsh, Genzyme Case Manager, elaborates:
As a Case Manager, I can verify benefits to get more information about all of the options available to patients and their families for coverage of Cerezyme. Individuals may have different out-of-pocket costs associated with their major medical and prescription benefits. Once we have a better understanding of an individual’s benefits, we can discuss how to best use them at their current infusion site with their current infusion provider.

For patients and families who are interested in looking into financial assistance for out-of-pocket costs, those who have commercial insurance are eligible to enroll in the Genzyme Co-Pay Assistance Program. This program provides reimbursement for drug-related and infusion-related out-of-pocket costs up to an annual maximum. Depending on how high an individual’s out-of-pocket responsibility is each year, I might also make a referral to another patient organization, such as the Patient Access Network (PAN) and National Organization for Rare Disorders (NORD). Both PAN and NORD offer financial assistance programs to eligible individuals for out-of-pocket costs associated with Cerezyme infusion. In some cases, a patient might receive assistance from one or more than one of these programs.

Question: I just received notice that I am losing my job. What should I do?

Answer, from Eileen Walsh, Case Manager:
We can work together to get more details on resources available to patients and their families in this situation. Paperwork provided by an individual’s employer can help determine when an individual’s benefits will end after he or she loses a job. This information is helpful because benefits include health insurance, which provides coverage for Cerezyme infusions. Once an individual has more information regarding his or her termination and how their benefits are being handled, we can look into all of the options available for health insurance. Individuals may qualify for continuation of their current insurance through COBRA, as well as other insurance plans such as Medicaid, an individual plan, or state-funded High Risk Pool plans. Once we have a better idea of the best option for an individual, I can refer him or her to a patient organization such as the National Gaucher Foundation (NGF), Patient Services, Inc. (PSI), or NORD, which offers premium assistance to eligible applicants. If we are unable to secure insurance quickly, I will work with the individual and his or her physician on possible assistance through the Genzyme Charitable Access Program. This program offers medication at no cost to approved applicants while we work together to secure coverage for their Cerezyme infusions.
Patient Profile

Herman Platt

By Cheryl Alkon

Whether it was being diagnosed with type 1 Gaucher disease at age 48, relocating to Florida after a lifetime spent in the Buffalo, New York area, or getting married for the first time at age 65, Herman Platt has faced late-in-life changes with aplomb.

“I think I have a pretty good life and it’s always getting better,” said Platt, now 71 and based in Cape Coral, Florida. “Most of it is associated with my wife, and it’s very different from my single days. Now that I’m retired, it has all come together to make my life exceptional.”

Diagnosis at 48

Platt’s life today doesn’t necessarily resemble his earlier years, but he’s alright with that. A lifelong bachelor living in Amherst, New York, Platt had been “feeling fine” when he went for a routine physical exam back in 1990. After the appointment, though, he received an unusual message.

“I got a call from the doctor’s office, and they thought their platelet counting machine was broken because my numbers were so low,” he said. “I went back again and the numbers were the same.”

Low platelet readings, called thrombocytopenia, can cause excessive bruising and can be a sign of type 1 Gaucher disease. But neither Platt nor his primary care doctor knew the cause, so Platt sought out a hematologist for more information.

The visit revealed an important diagnosis: Platt had type 1 Gaucher disease, a condition that occurs when the body cannot process fatty substances due to a lack of the enzyme glucocerebrosidase. The fatty substances build up and can cause problems in the liver, spleen, and bone marrow. In 1990, though, said Platt, “no one had ever heard of it.”

Beginning Treatment

Platt wanted more details and reached out to those who could offer help.

“I was going out with a woman at the time who was an attorney, and she took me to the nearby University of Buffalo library to do research online,” he said. In those years, it wasn’t possible to do such research on home computers; Google was still years away. Trained to do research with legal databases, his friend uncovered some crucial information. “She found a reference to Gaucher disease, and there was a reference to a drug that had just been approved, which was Ceredase® [algglucerase for injection],” Platt said.

Genzyme’s Ceredase, approved by the US Food and Drug Administration in 1991, was a first-generation infusion medication for type 1 Gaucher disease. (It was later replaced in 1994 by Cerezyme® [imiglucerase for injection].) (See Important Safety Information, page 2, and Product Information, centerfold.)

Platt searched for a local doctor to administer Ceredase treatment, and eventually connected with the late Zale Bernstein, MD, who was a hematologist and medical director of the Hemophilia Center of Western New York, in Buffalo.

“At the time, Ceredase was the drug of choice—the only one, actually—and my insurance company balked at the thought of paying so much money for it,” Platt said. His insurance company required that Platt drive to Albany, a 3.5-hour drive away, for a second medical opinion. “I brought a fistful of records, and the doctor spent 10 or 15 minutes with me,” Platt recalled. “He didn’t do more than what my own primary care doctor had done.”

However, the second doctor’s report convinced Platt’s insurance company that Ceredase could help. He began infusion therapy in Bernstein’s office, twice a month for two-hour sessions.

By that time, Platt was beginning to feel the effects of his untreated disease. “There was one period I looked terrible, and I was feeling really down,” he recalled. “I felt awful for a few months, but it started to turn around.”

Yet Platt knew that his disease was relatively mild. “I was an avid racquetball player, prior to the Gaucher discovery,” he said. “This friend and I played ‘angry racquetball’—think of it: two single angry men. I would get welts on my back that would last for a week at a time.” However, the welts never hemorrhaged, which is a potential effect of type 1 Gaucher disease. “I was fortunate I wasn’t a bleeder,” Platt said.

Therapy Differences

Platt’s flexible schedule allowed for ongoing infusion therapy. He was the director of his department. For 36 years, he oversaw the media resources department for Niagara University in Western New York until he retired in 2008.

He had a positive experience with infusion therapy. The Buffalo site was comfortable, and whenever he was there, Platt would have his own nurse caring for him, he recalled.

“As far as the medication is concerned, it works, and that’s all,” he said. “To me, it’s an opportunity to lay back and relax. My sister thinks, ‘Oh, you poor guy.’”
But infusion therapy allowed him to continue living life the way he wanted. “I was pretty active doing stuff with no ill effect that I could tell,” he said. “I never had to stop doing what I was doing, other than having to keep doing infusions.”

When Platt moved to Florida in 2010, he found local providers, as well as a doctor about three hours away who was doing research on an oral medication for type 1 Gaucher disease. At first, Platt met with the researcher, but wasn’t interested in enrolling in the study because it required regular visits and testing at an office roughly 140 miles away, in Coral Springs, Florida. Instead, he began infusion therapy at a location near his home that also provided chemotherapy to cancer patients.

Now, though, Platt is two years into an ongoing study overseen by Neal Weinreb, MD, analyzing the effectiveness of eliglustat, an experimental oral medication, and how it compares to Cerezyme. Platt takes the medicine at home twice a day. “I’m pretty rigid about taking it 12 hours apart,” he said. “I have alarms to catch my attention.”

He also travels three hours every few months for the research team to analyze the effectiveness of the medication, through blood work, magnetic resonance imaging scans, and other tests to analyze potential bone changes and other symptoms common in patients with type 1 Gaucher disease.

Though he was initially seeking a more comfortable form of treatment, Platt recognizes how his role in the research may benefit others.

“I may be helping a lot of other people,” he said. “Eventually it will be a lot more convenient just to take an oral medication. Good for them—let’s make it happen.”

**Lasting Love**

A lifelong bachelor, Platt had never wanted to get married. But after ending one five-year-long relationship, he turned to an online dating service in 2002 to explore.

“I was poking around on the computer and clicked on [the dating service website], and didn’t know what it was,” he said. “I thought it could be fun.” He typed in his zip code and was astonished by the results.

“I was really surprised at the pages of women who were making themselves available, with a photo, just 10 miles away,” Platt said. “I thought, ‘Maybe there’s one for me in Buffalo.’”

One woman’s photo and profile, Mary-Teresa, appealed to him, so he emailed her. She responded. Over several weeks, they emailed and instant messaged until they agreed to meet in person. The connection was instant.

“After we met, we came to find out that we went to the same grade school, and lived blocks apart, even though she is ten years younger than me,” said Platt. “We were in college at the same time.”

The couple dated for a long time. Despite his longtime aversion to marriage, friends urged him to propose marriage to Mary-Teresa.

“I have a couple of buddies I play pinochle [a card game] with, who I have played with for 30 years,” he said. “They would tell me I should marry this girl. And I came to realize my caring and loving was a pretty good thing.”

Ultimately, though he deemed it neither “original nor cool,” Platt took Mary-Teresa to a fancy restaurant “for no reason at all,” and handed her a card “that was so appropriate, and I wrote, ‘Will you marry me?’”

She looked at the card, looked at Platt, and said, “Are you sure you know what you’re doing?” Then she agreed.

Married since 2007, Platt’s happiness is obvious. “I just got lucky, you know,” he said. “It had to be something pretty powerful to make me change my ways.”

Feeling fortunate is how Platt views his type 1 Gaucher disease as well. “I’m lucky, my type 1 is really on the mild side, so it’s difficult to offer any kind of advice for others except to find out as soon as possible,” he said. “That means testing.”

“If you know someone in your family is a Gaucher carrier, or has the disease, getting tested gives you an opportunity to deal with it,” he added. “If you have it, you can take care of yourself. If you’re a carrier, you learn that this is an important thing to know.”

And if testing means type 1 Gaucher disease might become a part of your life at some point, the knowledge means you can get treated as soon as possible. And such treatment might just be the difference, in Herman Platt’s words, between a pretty good life or one that’s exceptional.

**Indications and Usage**

Cerezyme® (imiglucerase for injection) is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of type 1 Gaucher disease that results in one or more of the following conditions: anemia (low red blood cell count), thrombocytopenia (low blood platelet count), bone disease, hepatomegaly or splenomegaly (enlarged liver or spleen).

**Important Safety Information**

Approximately 15% of patients have developed immune responses (antibodies). These patients have a higher risk of an allergic reaction (hypersensitivity). Use Cerezyme® (imiglucerase for injection) carefully if you have had an allergic reaction to the product in the past. Symptoms suggestive of allergic reaction happen in 6.6% of patients, and include anaphylactoid reaction (a serious allergic reaction), itching, flushing, hives, an accumulation of fluid under the skin, chest discomfort, shortness of breath, coughing, cyanosis (a bluish discoloration of the skin due to diminished oxygen), and low blood pressure. Side effects related to Cerezyme administration have been reported in less than 15% of patients. Each of the following events occurred in less than 2% of the total patient population. Reported side effects include nausea, abdominal pain, vomiting, diarrhea, rash, fatigue, headache, fever, dizziness, chills, backache, and rapid heart rate. Because Cerezyme therapy is administered by intravenous infusion, reactions at the site of injection may occur: discomfort, itching, burning, swelling or uninfected abscess. Cerezyme is available by prescription only. For more information, consult your physician. To learn more, please see the enclosed full product information or contact Genzyme at 1-800-745-4447 (option 2).

**Please see accompanying full Prescribing Information on pages 9-10.**
Gaucher Disease
Type 1 Gaucher disease (pronounced go-SHAY) is a progressive, genetic disorder that causes many different symptoms. A person with Gaucher disease can’t produce enough of an essential enzyme called glucocerebrosidase (pronounced GLOO-ko-SER-e-bro-sy-daze), which breaks down a fatty substance called glucocerebroside.

Treatment with Cerezyme
Cerezyme replaces the missing enzyme in Type 1 Gaucher disease. Cerezyme is a modified form of glucocerebrosidase, created using recombinant DNA technology.
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Living with Cerezyme

If you have Type 1 Gaucher disease, taking care of your overall health is especially important. Coping with Type 1 Gaucher symptoms like fatigue, pain, and changes in physical appearance may seem overwhelming at times. But, in addition to sticking with Cerezyme treatment, there are some simple steps you can take to help manage your symptoms.

Resources

Getting reliable information, finding support for yourself, and identifying treatment centers with expertise in Type 1 Gaucher disease are all critical in managing the disorder. In this section, you will find sources for all these avenues of support.

Horizons

The Horizons newsletter helps Gaucher patients and their families stay connected to the larger Gaucher community. Horizons provides a wealth of information on Type 1 Gaucher disease, often written in collaboration with physicians, researchers, and other Gaucher experts.

Cerezyme Co-pay Assistance Program

The Genzyme Co-Pay Assistance Program helps eligible individuals in the United States who are prescribed treatment with Cerezyme pay for their eligible out-of-pocket drug and infusion-related expenses, including co-pays, co-insurance and deductibles, regardless of financial status.

Indication & Usage

Cerezyme® (imiglucerase for injection) is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of Type 1 Gaucher disease that results in one or more of the following conditions:

a. anemia (low red blood cell count)

b. thrombocytopenia (low blood platelet count)

c. bone disease

d. hepatomegaly or splenomegaly (enlarged liver or spleen)

Important Safety Information

Approximately 15% of patients have developed immune responses (antibodies). These patients have a higher risk of an allergic reaction (hypersensitivity). Use Cerezyme® (imiglucerase for injection) carefully if you have had an allergic reaction to the product in the past. Symptoms suggestive of allergic reaction happened in 6.6% of patients, and include anaphylactoid reaction (a serious allergic reaction), itching, flushing, hives, an accumulation of fluid under the skin, chest discomfort, shortness of breath, coughing, cyanosis (a bluish discoloration of the skin due to diminished oxygen), and low blood pressure.

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Cerezyme is available by prescription only. For more information, consult your physician.

Please see accompanying full Prescribing Information on pages 9-10.
Genzyme Co-Pay Assistance Program

Cerezyme® (imiglucerase for injection)

Get Started Today in

3 Easy Steps!

1. You complete the program application
   For more information about the program and to complete the online application, please visit: www.cerezyme.com/copay.aspx
   You can also call your Genzyme Case Manager directly to learn more about the program and application process at 1-800-745-4447, Option 3

2. Your Genzyme Case Manager verifies eligibility
   Your Genzyme Case Manager will review your application to verify eligibility.
   If you are eligible, you will be automatically enrolled in the program.
   Enrollment in the program is subject to confirmation of eligibility.

3. You’re enrolled
   Once approved, you will receive confirmation from your Genzyme Case Manager and an enrollment card will be mailed to you within 7-10 days.
   Your doctor or specialty pharmacy will also receive a confirmation letter with instructions on how to submit claims for reimbursement through the program.
   Your enrollment in the program is effective from the date of approval through the end of 2012.

Genzyme reserves the right to make eligibility determinations, to set program benefit maximums, to monitor participation, and to modify or discontinue the program at any time.

Genzyme Co-Pay Assistance Program

The Genzyme Co-Pay Assistance Program will help eligible individuals who are prescribed treatment with Cerezyme® (imiglucerase for injection) with their eligible drug related out-of-pocket expenses, including co-pays, co-insurance and deductibles, regardless of financial status.

Once enrolled in the Genzyme Co-Pay Assistance Program, Genzyme will pay 100% of your eligible out-of-pocket Cerezyme drug costs up to the program maximum. The 2012 Co-Pay Program runs from January 1, 2012 through December 31, 2012.

Who is eligible for this program?
Regardless of financial status, the program is open to individuals who are:
• U.S. citizens or legal residents who have primary commercial insurance
• Prescribed treatment with Cerezyme® (imiglucerase for injection)

Who is NOT eligible?
As required by law, the program is not available to individuals who:
• Are residents of Massachusetts
• Have coverage or prescriptions paid for in part or full under any state or federally funded healthcare program including:
  - Medicare
  - Medicare Advantage Plans (Example: FreedomBlue offered through Blue Cross Blue Shield)
  - Medicaid
  - Medigap
  - Veterans Affairs, Department of Defense or Tri Care
  - High Risk Pool or Pre-existing Condition Insurance Plan (PCIP)

Please call your Case Manager if you have any questions about your eligibility. If you are not eligible for our Co-Pay Assistance Program and need help with your out-of-pocket expenses, your Genzyme Case Manager is available to help review your coverage options and refer you to other financial assistance programs that may offer financial support for eligible individuals.

Genzyme reserves the right to make eligibility determinations, to set program benefit maximums, to monitor participation, and to modify or discontinue the program at any time. This program assists patients with their out-of-pocket Cerezyme drug costs only, not the cost of infusions, medical evaluations/appointments, testing, or other related services.

For full Prescribing Information for Cerezyme® (imiglucerase for injection) go to www.cerezyme.com