

Horizons

A Newsletter for the Gaucher Community From the Genzyme Corporation



Bone Health in Gaucher Disease Type 1

**Online Discussion Group Gives Valuable Support to
Patients With Gaucher Disease**

**Eliglustat Tartrate: An Oral Medication Under
Investigation for Adults With Type 1 Gaucher Disease**

An interview with Oved Amitay

Patient Connection

Warren McCollom

www.cerezyme.com

Contents

Eliglustat Tartrate: An Oral Medication Under Investigation for Adults With Gaucher Disease Type 1 (An interview with Oved Amitay)	3
The New and Improved Gaucher Registry	5
Bone Health in Gaucher Disease Type 1	7
Funding & Foundations (research and development costs for Gaucher disease type 1)	10
Online Discussion Group Gives Valuable Support to Patients With Gaucher Disease	12
Patient Connection: Warren McCollom	14

Foreword

Choices and options are important to patients with Gaucher disease type 1, says *Oved Amitay* in our exclusive interview with him about eliglustat tartrate, an oral investigational medicine being studied in patients with Gaucher disease type 1. Currently three studies — ENGAGE, ENCORE, and EDGE — are ongoing and open for enrollment. Amitay provides further information about these studies for patients who may be interested in participating. Potential new medications are not the only thing driving research in the treatment of Gaucher disease type 1, a new Gaucher Registry is currently being redesigned, updated, and enhanced to serve physicians and patients faster and more completely than ever before; an article by Elizabeth Barton in this issue of *Horizons* provides important specifics about the Registry updates. The information that patients and doctors provide to the Registry may contribute to more effective diagnostic approaches and improved disease intervention methods. Patients and doctors can access the Registry online. Patients looking for online comradery can find support by visiting the Yahoo! Gaucher Disease Discussion Group, detailed in this issue thanks to Talya Raveed, a Gaucher peer who struggled as a young child with the painful and mysterious symptoms of Gaucher disease type 1 and today is a retired nurse, who lends her support to users on the Yahoo! Discussion Group. But that’s not all you will find in this issue of *Horizons*. The “Funding & Foundations” section provides information on The National Gaucher Foundation and looks at the costs involved in enzyme replacement therapy. This issue includes an in-depth article from leading expert Neal Weinreb, MD, that looks at the skeletal complications and bone health in Gaucher disease type 1. Once you have had a chance to look at the articles in this issue, send us a note with your feedback, so that you too can help shape your own *Horizons*.

—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, thrombocytopenia, bone disease, hepatomegaly, splenomegaly.

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 (enclosed).

Patients are encouraged to report negative side effects of prescription drugs to the FDA. Visit FDA.gov/medwatch, or call 1-800-FDA-1088.

Eliglustat Tartrate: An Oral Medication Under Investigation for Adults With Gaucher Disease Type 1

An interview with Oved Amitay

Last year, Genzyme presented new data on eliglustat tartrate, an investigational oral medication for Gaucher disease type 1, at the 6th Annual Symposium on Lysosomal Storage Diseases, held in Miami, Florida. *Horizons* conducted an in-depth interview with Oved Amitay, vice president and general manager of the Gaucher Disease Portfolio at Genzyme.



Is Genzyme conducting any new research for patients with Gaucher disease type 1?

Oved: Genzyme has a history of research for, and commitment to, the Gaucher disease community. About 10 years ago, we started to recognize the impact that enzyme replacement therapy had on the lives of patients with Gaucher disease type 1. We also recognized that the continual intravenous infusions of enzyme replacement therapy required to keep patients with Gaucher disease type 1 well balanced may be a challenge for some patients. Choices and options are important to patients with Gaucher disease type 1, so, with that recognition, Genzyme began developing eliglustat tartrate, an oral investigational medicine, to study in patients with Gaucher disease type 1.

What is eliglustat tartrate?

Eliglustat tartrate is a substrate reduction therapy. It is believed to decrease the production of the fatty substance (glucosylceramide) that accumulates in Gaucher disease type 1 by decreasing the activity of the enzyme (glucosylceramide synthase) that produces the fatty substance. Eliglustat tartrate was designed to specifically target this enzyme.

In a Phase 2 study, the primary goal was to see if eliglustat tartrate had an effect on organ size, red blood cells, and platelets. At 1 year, the Phase 2 study met its

primary goal endpoint. One patient experienced irregular heartbeats; other drug-related side effects included infrequent abdominal discomfort, diarrhea, headache, and transient heart palpitations (sensation of a pounding increase in heart beat). Each of these events occurred in 1 or 2 patients, was mild, and lasted only a short time.

Although taken orally, eliglustat tartrate should not be confused with Zavesca® (miglustat), another oral compound already commercially available in some countries.

Why has it taken so long for Genzyme to investigate other compounds for the treatment of Gaucher disease type 1?

Developing drugs, in general, takes a long time. It takes about 7 to 8 years to get a drug from the chemical stage to the final stages of clinical studies. It also takes a lot of money. Unfortunately, it gets so complicated and so expensive that fewer and fewer companies are actually able to develop new drugs. That is one of the challenges for the entire healthcare system: How can we develop new drugs more efficiently? How can we do it in a way that won't compromise safety and efficacy, but still get it done in a reasonable timeframe?

The challenges of working with a rare disease are more complicated and profound. In the case of Gaucher disease type 1, it becomes even more difficult to find patients who are willing to participate in clinical studies when there are already treatments available on the market that are safe and efficacious.

What clinical research studies is Genzyme currently conducting for patients with Gaucher disease type 1?

There are three studies — ENGAGE, ENCORE, and EDGE — ongoing and open for enrollment. Collectively, these studies are the Explorer Studies, and together they represent the largest studies of Gaucher disease ever conducted.

These trials are designed to evaluate if the investigational oral medication eliglustat tartrate is safe and effective in the treatment of Gaucher disease type 1 signs and symptoms.

Participation in these studies may help us more effectively treat patients with Gaucher disease in the future.

ENCORE Study

The primary goal of the ENCORE study is to assess the safety and effectiveness of eliglustat tartrate compared to imiglucerase for injection, a commercially available enzyme replacement therapy (ERT) after 12 months of treatment in patients previously treated with ERT who have met therapeutic goals. Participants will be assigned to one of two groups: those who will receive the investigational oral medication, eliglustat tartrate, or those who will be treated with imiglucerase for injection. After 1 year in the study, all participants will receive eliglustat tartrate twice daily until it becomes commercially available or the study closes.

ENGAGE Study

The primary goal of the ENGAGE study is to assess the safety and effectiveness of eliglustat tartrate compared to placebo after 9 months of treatment in untreated patients with Gaucher disease type 1. Participants will be assigned to one of two groups: eliglustat tartrate or placebo (a capsule with no active ingredient), twice daily. After 9 months in the study, all participants will receive eliglustat tartrate twice daily until it becomes commercially available or the study closes.

In the case of Gaucher disease type 1, it becomes even more difficult to find patients who are willing to participate in clinical studies when there are already treatments available on the market that are safe and efficacious.

EDGE Study

The EDGE study is comparing once-daily to twice-daily dosing of eliglustat tartrate. Eligible participants will be treated with eliglustat tartrate twice daily for at least 6 months and then be randomly assigned to receive either once-daily or twice-daily dosing for 12 months.

To learn more about the Explorer Studies, please visit www.explorerstudies.com or visit www.clinicaltrials.gov. Participation in these studies may help gather information to more effectively treat patients with Gaucher disease type 1 in the future. ■

Genzyme Care Coordination

Genzyme Case Managers offer comprehensive, free and confidential care coordination services including:

Educational Information:

- Information about Type I Gaucher disease
- Information about medical experts
- Identify treatment sites in your area
- Information about treatment with Cerezyme® (imiglucerase for injection)
- Learn about the Gaucher Registry
- Information about testing

Insurance Assistance:

- Assist in obtaining and maintaining health insurance coverage
- Examine your policy's lifetime maximum benefit
- Identify alternative funding resources
- Billing and claims support, including appeals
- Assist with insurance transitions such as loss of job, college, marriage, disability, retirement & job changes

For almost 20 years, Genzyme has provided individualized case management to people living with Type I Gaucher disease and their families.

Haven't tried our services?

Simply call 1-800-745-4447 option 3 for a one-on-one consultation with a Case Manager in your area. Find out what Genzyme Care Coordination has to offer.

1-800-745-4447 option 3
Your Call, Our Commitment

You do not need to be on or seeking treatment with Cerezyme® to access Genzyme's free and confidential services.



The New and Improved Gaucher Registry

By Elizabeth Barton

The Gaucher Registry, originally established in 1991, is currently being redesigned, updated, and enhanced to serve physicians and patients faster and more completely than ever before.

The Registry is the first and largest database to promote an understanding of the progression of Gaucher disease and track the outcomes of clinical practices. It gives physicians access to useful information and helps patients better understand their own treatment goals.

According to Richard Moscicki, chief medical officer, senior vice president Biomedical & Regulatory Affairs at Genzyme Corporation, the pharmaceutical company sponsoring the program, “the fundamental goals of the Gaucher Registry are two-fold: to advance the medical and scientific understanding of Gaucher disease; and to improve the quality of care of patients around the world through the publication of data and development of evidence-based disease management guidelines.”

Generally, disease registries are large, multinational databases that medical professionals use to collect clinical data on disease progression and treatment response from patients with a particular disease. Because Gaucher disease is so rare, creating and maintaining a reliable, comprehensive registry for physicians and patients has been of paramount importance.

The Gaucher Registry is now being redesigned using an innovative Web-based data collection and reporting system. “The main objective of this project is to use this new technology to further increase knowledge and improve patient outcomes,” Moscicki said. “We wanted a system that helped physicians and their patients look at longitudinal data in a more efficient and systematic way,” he said.

Importance of the Gaucher Registry

The database helps improve patient care by allowing physicians to monitor patient information, track individual case reports, and view long-term effects of treatment. As a result of the database’s collective capabilities, healthcare professionals and disease specialists can submit and access clinical information about the disease. This streamlined method of information sharing assists research and may help improve diagnostic approaches and disease intervention methods throughout the world.

Chris Jones, director of the Lysosomal Disease Registry Platform, emphasized that the Registry is separate from Genzyme and its marketing efforts. “Genzyme is the custodian of the Registry—we don’t drive the science. An independent board, known as the International Collaborative Gaucher Group, governs the medical and scientific agendas of the Registry. We put a lot of effort into properly maintaining the continuity of information on the Registry.”

Information and Education

“The idea for the redesign came about through a project done a couple of years ago studying what patients want online,” said Moscicki. “Patients were very interested in increasing their access to patient case reports. So it’s very important for patients to support the Registry because they are contributing to the research of the disease. Patients are the heart of the Registry.”

Anyone with Gaucher disease, regardless of whether or not he or she is undergoing disease-specific treatment, is encouraged to participate. “Patients should be referred to their physicians if they are interested in the Registry, and the physician can then invite the patient to participate,” explained Jones.

Patients will be able to easily access information, explained Jones. “Patients will now be invited to set up an account and view their report. The Registry provides them with a visual representation of how they are doing over time, such as information on their platelet levels and how their bones are doing. It gives patients a view of their disease status, along with comments from their physicians.”

Another new feature is the ability for patients to set up a care team, which would invite all of the patient’s physicians

“...it’s very important for patients to support the Registry because they are contributing to the research of the disease. Patients are the heart of the Registry.”

—Richard Moscicki



to participate. Patients can then view the data that their physicians shared.

Secondary teams, or additional team members or specialists, can participate along with an existing registry team. Based on his or her physician's discretion, a patient may access specific clinical reports. The Registry's new, easy-to-read graphical presentation of information also will promote the participant's understanding of the statistical analysis and individual developments, and the customization options will help tailor the information to suit the patient's needs.

Total Patient Privacy

The patient's privacy and confidentiality are strictly maintained in compliance with national privacy regulations and applicable state or local laws regarding medical data. To further protect patient confidentiality, the information submitted to the Registry references the patient only by his or her initials and Registry-issued ID number.

"The data actually will be even more secure because users will be able to transfer documents by logging in to the secure site rather than sending them through the mail, and there also will be encryption," explained Jones.

The care that each Registry participant receives at regular doctor visits will be unaffected; the only difference is that the medical information the physician collects (such as information regarding the patient's organs, bone health, and quality of life) will be uploaded to the Registry. Patients may discontinue their involvement in the Registry at any time.

The Next-Generation Workings

The Registry will be powered by the RegistryNXT! Platform. RegistryNXT! is the patient-focused platform for the Lysosomal Storage Disease (LSD) Registries, including the Gaucher Registry, and will grow to include Pompe, Fabry,

and Mucopolysaccharidosis I (MPS I) in the next few years. The streamlined method of information sharing facilitated by RegistryNXT! may contribute to more effective diagnostic approaches and improved disease intervention methods.

"The new program is going live right now with ten sites, and the rest of the sites are rolling out globally in early 2011. Everyone will be on the new system in 2011," according to John Yee, MD, vice president of evidence-based medicine at Genzyme Corporation.

Initial sites will receive training, provide feedback, and uncover any technical bugs, and the transition will later expand to include all sites as they begin to move to the new system in 2011. In time, all of the LSD Registries will be integrated, with the Pompe Registry next.

Improved Registry Features

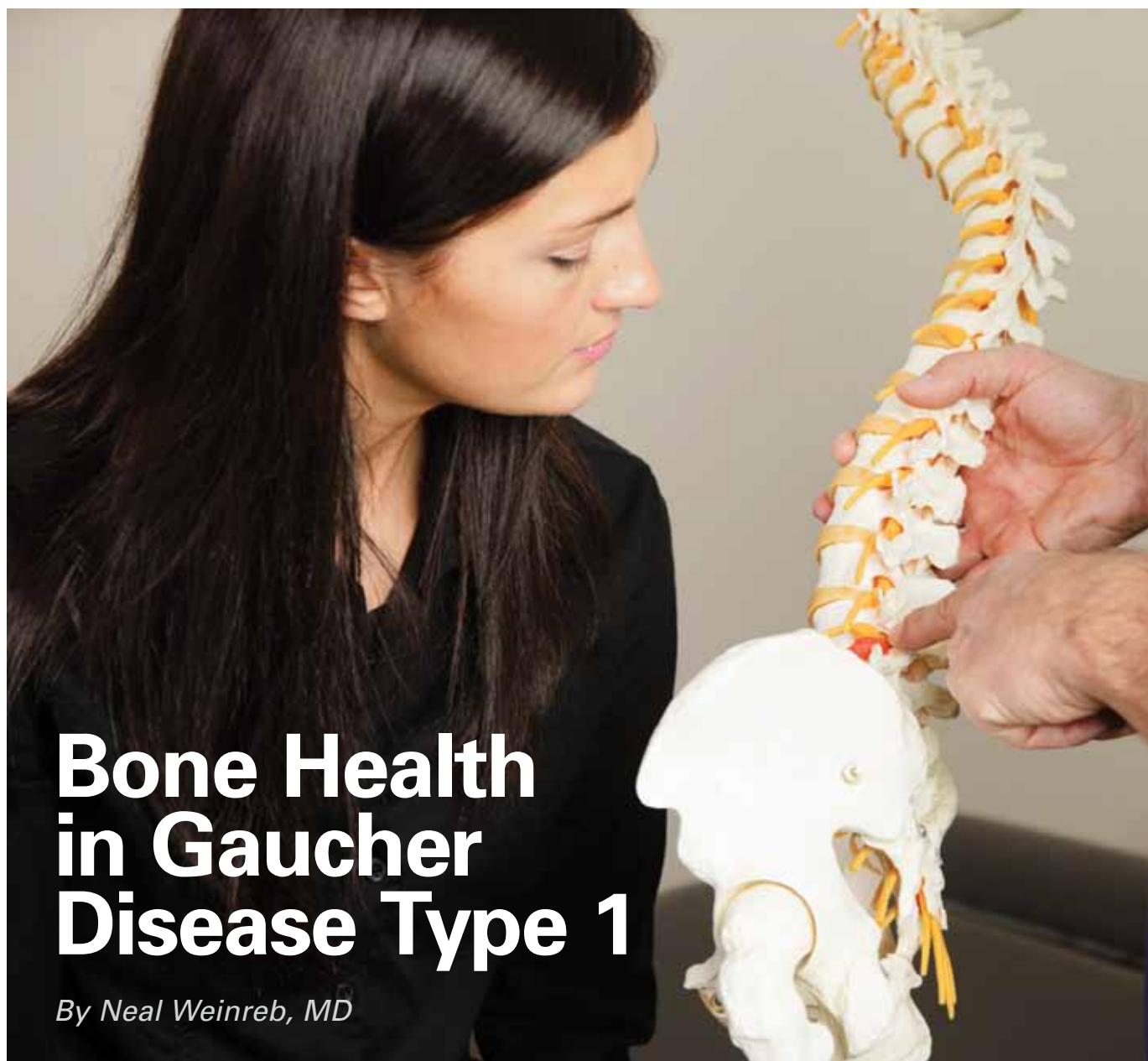
The data collection tool is entirely Web-based, so no installation is required, and the process will promote a patient care-focused system. Strict adherence to industry standards, wherever possible, improves Case Report Form (CRF) consistency. The data-entry process will be easier and more complete with the use of task lists and pull-down menus, and updated information will be accessible instantly through improved data-reporting speed. Data sharing will take place in real time, which is a considerable enhancement from the previous Registry publication system, which was updated only once a month in a PDF file.

The Dashboard feature tracks the progress of each patient's data and displays tasks to be completed. The new platform will update Patient Case Summaries (PCRs) in near real-time and permit the user to download select data directly into Excel at any time. The PCR also will include a graphical summary of the patient's history that is easy to read, interactive, and sharable. The graphs can be quickly and easily adjusted to suit the user's needs. The Registry's tools can filter reports using different data sets—at a specific site, regionally, or globally. The interactive nature of the PCR will allow individual patient data and treatment progress to be easily compared to those of other patients.

Benefit to Worldwide Community

The worldwide collaborative capabilities of the Gaucher Registry stand to benefit the entire disease community. With rare diseases, one can only answer questions when the data are assembled from many different sources, and the Registry will aid the expansion and dissemination of all of this accumulated information. Professionals with interests in the disease, but not currently treating patients, qualify for "affiliate" status that would allow them to access select registry data.

To date, the Gaucher Registry is approaching 6000 patient participants from more than 60 countries. To learn more about the enrollment process, visit the Registry website at www.gaucherregistry.com.



Bone Health in Gaucher Disease Type 1

By Neal Weinreb, MD

Before enzyme replacement therapy became available nearly 20 years ago, people with Gaucher disease type 1 commonly suffered bone pain on a daily basis, sometimes punctuated by sprained or broken bones that left them suffering and unable to function independently. They often lived their lives in wheelchairs or needed walkers or canes to get around, never knowing when they might break a bone or have their hips, knees, or shoulders fail.

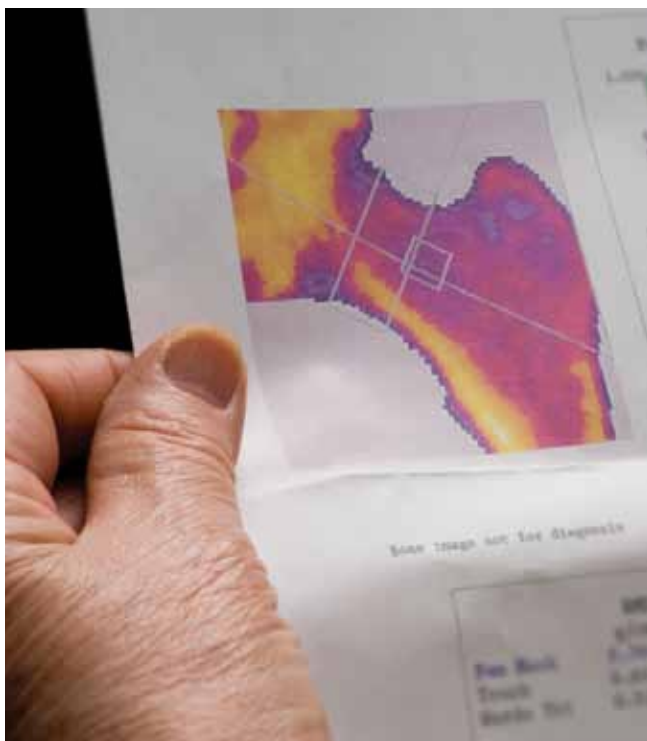
Although Cerezyme® (imiglucerase for injection) treatment has been shown in registry data to improve the bone strength and mobility of many patients with Gaucher disease type 1,¹ more than 80% of patients still have evidence of bone involvement that can cause serious, even life-altering skeletal and joint conditions.² For example, patients who suffered irreversible bone complications before starting Cerezyme treatment have an ongoing need for expert orthopedic, rehabilitation, and pain management. Patients in countries with less access to health care can also develop serious bone complications because of delays in treatment. Moreover, patients currently being treated with Cerezyme need to attend regular monitoring appointments to ensure that they achieve their therapeutic goals.

Issues Related to Skeletal Involvement

Growth retardation in children: Children who have signs and symptoms of Gaucher disease type 1 are often much shorter than nonaffected children, even nonaffected siblings of the same age. Although most of these children eventually catch up to their peers (usually with onset of puberty, which itself may be delayed), the short stature can pose a social disadvantage, and affected children can experience teasing from other children.

A real challenge, however, relates to the increased frequency with which Gaucher disease type 1 is being diagnosed in children who don't show any symptoms. More diagnoses occur these days, either because of newborn screening programs or because of diagnosis in a brother or sister. In these circumstances, especially in clinically milder types of the disease, it is hard for doctors to predict the child's growth pattern or, for that matter, what signs or symptoms of Gaucher disease type 1 he or she may experience. Such children also need follow-ups, so that if growth disturbances or other signs of Gaucher disease type 1 arise, they can receive the appropriate treatment.

Poor bone mineralization (osteopenia, osteoporosis) and risk for fracture: Fractures (broken bones) with little trauma or even spontaneous fractures often took place in patients with Gaucher disease type 1, prior to enzyme replacement therapy. In some cases, these fractures occurred in bones weakened by focal (or spotty) areas of bone breakdown called *lytic lesions*.



Nowadays, lytic bone lesions occur less frequently, possibly because treatment is started earlier in patients with symptoms, and also because doctors are performing fewer splenectomies (surgical removal of the spleen). Aside from lytic lesions, bone strength in patients with Gaucher disease type 1 is more commonly weakened because of a generalized "thinning" of the bones, known in its milder form as *osteopenia* and in its severe form as *osteoporosis*.

Registry data indicate that osteopenia or osteoporosis occurs in 50% to 60% of adult patients with Gaucher disease type 1, and in an even larger percentage of elderly patients, especially women. However, a recent study from the International Collaborative Gaucher Group (ICGG) Registry indicates that the process of poor bone formation and mineralization that leads to osteopenia/osteoporosis often begins during childhood and adolescence.³ As a result of this early effect of Gaucher disease type 1, untreated individuals generally do not achieve a peak level of bone mass in young adulthood. Bone loss is common in aging humans, and patients with Gaucher disease type 1 who have begun at a lower level of bone mass end up having lower bone mineral density (BMD) scores than so-called "normal" individuals.

Registry data showed that BMD improved with Cerezyme[®] (imiglucerase for injection) treatment, and the greatest affects were seen in children, teenagers, and young adults.² Thus, doctors need to watch closely for evidence of low BMD in *all* patients with Gaucher disease type 1. The most common test for BMD is called DEXA (dual-energy x-ray absorptiometry) and is commonly available in most parts of the developed world. Because the standards are different for children than for adults, children and teenagers should have DEXA testing done only at centers that have specialists who are experienced in pediatric testing.

Although a number of treatments are used for osteoporosis, especially in postmenopausal women, the ones used most commonly are the bisphosphonates. So far, doctors and researchers still don't know if bisphosphonates decrease fracture risk in patients with Gaucher disease type 1 as they do in non-Gaucher, postmenopausal women. Large numbers of patients are needed for studies that look at decreases in fracture risk, and the Gaucher type 1 population is very small, therefore, it is extremely difficult to collect enough patients to do a clinical trial with proper statistical power.

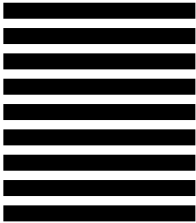
Because of complications associated with bisphosphonates, doctors need to be cautious when prescribing them to Gaucher type 1 patients.

Bone pain and bone crises: Historically, more than 50% of patients with Gaucher disease type 1 have chronic bone pain. The cause is somewhat obscure, but may be related to infiltration of the bone marrow with Gaucher cells that secrete chemicals that can lead to inflammation. It can be difficult to distinguish Gaucher type 1 bone pain from other pains of the muscles, tendons, and joints that can occur not only in patients with Gaucher type 1, but in other people as well. Registry data have shown that Cerezyme[®] (imiglucerase for

Intellisphere, LLC



NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES



BUSINESS REPLY MAIL
FIRST-CLASS MAIL PERMIT NO. 16 PLAINSBORO, NJ

POSTAGE WILL BE PAID BY ADDRESSEE

Attn: Sandra Kear
Intellisphere, LLC
Office Center at Princeton Meadows
666 Plainsboro Road
Building 300, Suite 300
Plainsboro, NJ 08536-9979





Cerezyme[®]
(imiglucerase for injection)

200 UNITS

400 UNITS

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 ($M_r = 60,430$). Imiglucerase differs from placental glucocerebrosidase by one amino acid at position 495, where histidine is substituted for arginine. The oligosaccharide chains at the glycosylation sites have been modified to terminate in mannose sugars. The modified carbohydrate structures on imiglucerase are somewhat different from those on placental glucocerebrosidase. 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:

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

*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 **DOSE 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[®] (alglucerase 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 \pm S.D., 14.5 \pm 4.0 mL/min/kg). The volume of distribution corrected for weight ranged from 0.09 to 0.15 L/kg (0.12 \pm 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:

- anemia
- thrombocytopenia
- bone disease
- 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[®] (alglucerase 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[®] (alglucerase 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. Pre-treatment with antihistamines and/or corticosteroids and reduced rate of infusion have allowed continued use of **Cerezyme**[®] in most patients.

Additional adverse reactions that have been reported in approximately 6.5% of patients treated with **Cerezyme**[®] include: nausea, abdominal pain, vomiting, diarrhea, rash, fatigue, headache, fever, dizziness, chills, backache, and tachycardia. Each of these events was found to occur in < 1.5% of the total patient population.

Incidence rates cannot be calculated from the spontaneously reported adverse events in the post-marketing database. From this database, the most commonly reported adverse events in children (defined as ages 2 – 12 years) included dyspnea, fever, nausea, flushing, vomiting, and coughing, whereas in adolescents (>12 – 16 years) and in adults (>16 years) the most commonly reported events included headache, pruritus, and rash.

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:

	200 Unit Vial	400 Unit Vial
Sterile water for reconstitution	5.1 mL	10.2 mL
Final volume of reconstituted product	5.3 mL	10.6 mL
Concentration after reconstitution	40 U/mL	40 U/mL
Withdrawal volume	5.0 mL	10.0 mL
Units of enzyme within final volume	200 units	400 units

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

U.S. Patent Numbers: 5,236,838
5,549,892

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.

6743 (4/05)



injection) treatments helped eliminate or reduce bone pain that was directly related to Gaucher disease type 1 itself.⁴ However, when patients have changes in their bones that cause permanent damage, neither Cerezyme nor any other Gaucher disease type 1-specific treatment will alleviate the pain of irreversible bone disease.

The key to the management of bone disease, with or without bone crises, is prevention. Registry data have shown that after institution of Cerezyme, the incidence of bone crises decreased. Two factors that make it more likely that patients may have recurrent bone disease after Cerezyme treatment is started are: 1) a history of prior splenectomy; and 2) a delay in initiation of Cerezyme after a diagnosis of symptomatic

Gaucher disease type 1 is established.⁴ Unfortunately, doctors cannot accurately predict which patients with Gaucher type 1 are at a higher risk of developing bone crises (the first episode can occur after many years without symptoms), but some risk factors may heighten their suspicion. These include a history of splenectomy, a diagnosis of Gaucher type 1 at a young age because of associated signs and symptoms, and presence of “unfavorable” genotypes.

Vigilance in Skeletal Care

Despite the fact that many people these days think of Gaucher disease type 1 as a disorder that primarily affects the blood, liver, and spleen, issues related to skeletal involvement in Gaucher disease type 1, such as growth retardation; poor bone mineralization and risk of fracture; and bone pain, bone crises, and bone disease still pose challenges and require the continued vigilance of both doctors and patients alike.

References

1. Sims KB, Pastores GM, Weinreb NJ, Barranger J, et al. Improvement of bone disease by imiglucerase (Cerezyme®) therapy in patients with skeletal manifestations of type 1 Gaucher disease: results of a 48-month longitudinal cohort study. *Clin Genet.* 2008;73:430-440.
2. Weinreb NJ. The bone in Gaucher disease. *Euro Musculoskelet Rev.* 2007;2:1-5.
3. Mistry PK, Weinreb NJ, Kaplan P, Cole JA, Gwosdow AR, Hangartner T. Osteopenia in Gaucher disease develops early in life: Response to imiglucerase enzyme therapy in children, adolescents and adults. *Blood Cells Mol Dis.* 2010 Nov 26. [Epub].
4. Charrow J, Dulisse B, Grabowski GA, Weinreb NJ. The effect of enzyme replacement therapy on bone crisis and bone pain in patients with type 1 Gaucher disease. *Clin Genet.* 2007;71:205-211. ■

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, thrombocytopenia, bone disease, hepatomegaly, splenomegaly.

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 (enclosed).

Funding & Foundations

Foundation of Hope

The National Gaucher Foundation (NGF) focuses on the needs of people living with Gaucher, their families, and caregivers. The NGF funds research, grants financial assistance, promotes education and awareness, supports legislation, and provides a variety of programs. Through the National Gaucher Care Foundation, the CARE Program, and the Care+Plus Program, NGF extends financial assistance to individuals with Gaucher disease. Supporting medical and lay-community outreach, NGF hosts live Webinars, national conferences, and patient forums. Its national and regional marketing programs also promote ongoing awareness of Gaucher disease. To learn more about the information and support services available from NGF, visit www.gaucherdisease.org.



Value of Enzyme Replacement Therapy

The average annual cost of enzyme replacement therapy is approximately \$200,000.¹ Dosage for these products is based on a patient's weight, meaning that the annual cost of treatment for children is less, and the cost for heavier adults is higher. Because so few people require these products, the overall cost to individual healthcare systems and insurance plans is small. Three principal factors help determine the cost of enzyme replacement therapy: research and development costs, manufacturing and distribution costs, and costs associated with the rarity of the condition that it treats.



Research and development costs: The costs to develop treatments for ultra-rare diseases such as Gaucher disease are just as high as for most other drugs on the market today (as much as \$500 million per product), but there are far fewer patients to pay for them.² Postmarketing commitments required by regulatory agencies mean that development costs can continue even after products are approved. Companies such as Genzyme continue to make significant investments in potential second-generation treatment approaches that could provide additional benefits for patients.

1. Adapted from Genzyme: The Cost of Enzyme Replacement Therapy. What contributes to the cost of these products? Available at: http://www.genzyme.com/commitment/patients/costof_treatment.asp. Accessed December 10, 2010.
2. Zitter M. Managing drugs for rare genetic diseases. *Managed Care*. 2005;14(2)52-64.

Is it worth the \$200,000 annual cost to treat Gaucher disease?

When a person suffers from a severe, progressively debilitating, and potentially fatal disease such as Gaucher disease type 1, the right treatment can reduce and even reverse the symptoms of the disease. Untreated, the disease can also be costly because it requires significant medical intervention. Fortunately, the products approved for treatment have broad reimbursement support in the United States and globally because of the clinical value they provide. It is hard to put a price tag on improved health.



What if patients cannot afford the therapy?

Approximately 10% of patients on Cerezyme® (imiglucerase for injection) enzyme replacement therapy receive the product for free. Genzyme provides Cerezyme free of charge through programs that include the Gaucher Initiative, a collaboration with Project Hope. Through this program, the drug is made available to patients in developing countries where government reimbursement has not been established.



Manufacturing and distribution costs: Creating an enzyme replacement therapy using recombinant DNA technology is among the most time-, labor-, and resource-intensive drug-manufacturing processes in use today. This type of manufacturing is far more costly than the manufacturing of a pharmaceutical pill. Genzyme invests hundreds of millions of dollars to build manufacturing plants to help ensure patients receive access to the products they need.¹ Services that add to the costs include patient advocacy and education, doctor training and referral networks, and local and regional case management.²

Rarity: The most significant factor affecting the cost of these treatments is the rarity of the diseases they treat. This may be due to the fact that development and manufacturing costs are supported by a patient population that is a small fraction of the population who use most drugs (**Table**). The US Orphan Drug Act of 1983, for example, defines a *rare disease* as one affecting fewer than 200,000 people in the United States. There are approximately 1500 patients with Gaucher disease type 1 in the US, which means that it is an *ultra-rare* disease.

Table. Diseases treated with biologic or injectable agents

Disease	US Prevalence
Psoriasis	5.8-7.5 million
Hepatitis C infections	3.9 million
Rheumatoid arthritis	2.1 million
Severe allergic asthma	500,000
Multiple sclerosis	400,000
<i>"Rare" is <200,000 as defined by Orphan Drug Act of 1983</i>	
Alpha-1 antitrypsin deficiency	100,000
Sickle cell anemia	91,000
Multiple myeloma	63,000
Cystic fibrosis	30,000
<i>"Ultra-rare" is generally defined as <10,000</i>	
Fabry disease	5000
Gaucher disease	2500
Tyrosinemia type 1	2500
Mucopolysaccharidosis (MPS 1)	200

Adapted from Zitter M. Managing drugs for rare genetic diseases. *Managed Care*. 2005;14(2)52-64.

Online Discussion Group Gives Valuable Support to Patients With Gaucher Disease

The Yahoo! Gaucher Disease Discussion Group,^a an online resource where patients with the disease can share information, has been an invaluable support tool for patients such as Talya Raveed.^b

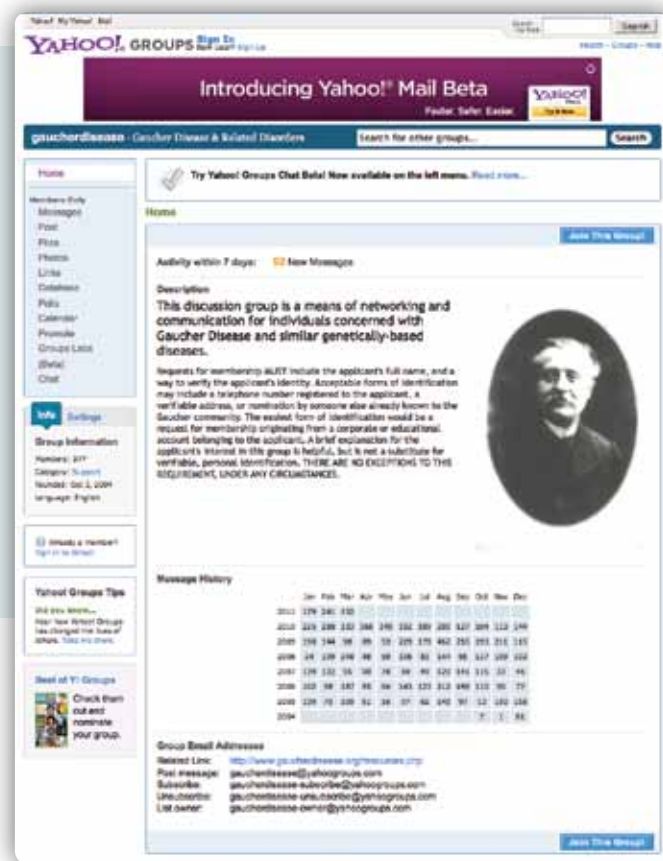
Wayne D. Rosenfield, PhD, a professional psychologist, founded the discussion group in 2004, although he first launched an earlier version a decade before that. Since then, the group has attracted about 1000 members, and currently has more than 400 from several different countries. Rosenfield, who also has Type 1 Gaucher disease, said that he envisioned the group as a source of crucial emotional support for people suffering with this disorder.

“Many people with Gaucher disease, myself included, have experienced the isolation and anxiety of a disorder that is rare and poorly understood by healthcare providers,” Rosenfield explained. “The growth of the Internet in the 1990s provided a very effective and cheap medium for connecting members of the Gaucher community anywhere in the world.”

To join the group, potential members must identify themselves, as well as their reasons for wanting to join, to the group’s moderators, who screen all applicants to ensure the group’s safety and integrity. Once accepted, members can log on to read posted messages, or sign up to receive posts by e-mail. Members can choose to remain anonymous to other participants simply by refraining from posting messages. Most of the members do choose anonymity, Rosenfield said, but a few actively share personal stories and information about living with Gaucher disease.

“Of course, you can be a member and just read the e-mails,” Raveed said, “but we would love to hear from you wherever you are. If English is not your first language, please don’t worry; we are more interested in you than your grammar.”

Raveed is one of the more active members. She reads the messages posted by others daily and willingly shares her own anecdotes and insights. The discussion group, she says, has provided her with invaluable information about managing



and treating the disorder. A sampling of some recent messages yielded information about vitamin D supplements, an upcoming national meeting, and a recent recall of a type of hip implant.

“This is a place where I learn what is new with Gaucher disease,” Raveed explained. “This is a place where we are happy to greet new members who often have just been diagnosed with Gaucher. This is a place to learn how individuals manage their Gaucher and share their experiences, find meetings—local and national—and this is also a great place to give and get support.”

The discussion group does not provide medical advice or consultation, and is solely a forum of peers. This is one of its greatest benefits, according to Rosenfield: Patients with Gaucher disease who join the group gain access to a community of other patients that they otherwise would never meet. Much like a traditional support group, the online

discussion group gives participants the opportunity to learn from each other's experiences.

"The members are able to share concerns or problems," Rosenfield said. "With the support and experience of hundreds of people dealing with similar problems, individuals find that they have the comfort of a peer community and the knowledge that comes from experience."

Joining the discussion group is a free, easy process that can begin on the National Gaucher Foundation (NGF) Web site (<http://www.gaucherdisease.org>). The discussion group is not affiliated with the NGF or any other companies, including Genzyme. From there, users can click on Programs, then the Genetic Disease Discussion List. Alternatively, patients can click on the green [Join the Listserv](#) button in the center of the NGF homepage. The direct link to the listserv is: <http://health.groups.yahoo.com/group/gaucherdisease>.

Once there, click on Join This Group, and follow the prompts. After being approved, usually a day or so after submitting an application, a confirmation e-mail is sent to

the new member, and the process is complete.

While the discussion group is geared toward people with Gaucher disease, it comprises the whole Gaucher community, including family members and friends of patients, doctors who treat the disease, and researchers studying its causes and treatment.

"For my future friends who have Gaucher, like myself, or who have family or close friends with Gaucher, the online discussion group is a wonderful place for us," said Raveed,^b adding: "I just think that everyone who has Gaucher deserves the gifts that this group delivers."

Genzyme has no affiliation with either the Yahoo Group or to these individuals.

^a<http://health.groups.yahoo.com/group/gaucherdisease>. The Yahoo! Gaucher Disease Discussion group is not owned by any person or company. Participation is voluntary, and members can choose to terminate their membership and leave the group at any time.

^bTalya Raveed is solely a member of the Yahoo! Gaucher Disease Discussion Group and had no founding role and has no current role in running the group. Talya Raveed and Wayne D. Rosenfield have no affiliation with Genzyme Corporation.

^cFor more information about this study, please go to: http://www.gaucherdisease.org/genzyme_drug_information2.php. ■

Talya's Story

At age eight, Talya Raveed began a frightening, 4-year journey to pediatricians and other medical specialists, including psychiatrists, seeking a diagnosis for a host of confusing symptoms. Among her ailments were bone pain, chronic fatigue, low-grade fever, and an enlarged abdomen. While many physicians today may recognize these symptoms as Gaucher disease type 1, when Talya was growing up in the 1960s, the disease was poorly understood, and a reliable diagnostic test was years away.

When Talya was age 12, she underwent surgery in Israel, which was then her home, to treat bone damage in her leg caused by insufficient blood flow — a serious condition that can affect patients with Gaucher disease type 1. During surgery, she had excessive bleeding that required a blood transfusion. Finally, after an extremely painful bone biopsy yielded abnormal results, Talya's search for the elusive cause of her symptoms ended. After years of misdiagnoses from other doctors, Talya's orthopedic surgeon in Israel diagnosed her with Gaucher disease type 1.

Now a 58-year-old retired nurse in Albuquerque, New Mexico, Talya continues to suffer pain from the disease that went untreated until treatment finally became available when she was in her 40s. She had a brother with Gaucher disease, as well, but, sadly, he died before receiving therapy for the disease. Her personal experience, as well as her professional career as a registered nurse specializing in clinical trials, has inspired Talya to help others who may be suffering with Gaucher disease find the support that she so lacked as a child.

"I am so happy that with treatment most people can avoid many of the health issues that I and many people my age suffered and continue to suffer," said Talya. "Now, thankfully, only a simple blood draw is needed to test for Gaucher disease and carrier status."



Patient Connection: Warren McCollom

By Nick Sambides Jr.

His left hip socket and his right knee have been surgically replaced, as have his right and left hips — twice. A Titanium mesh cage couples two vertebra of his spine. Bones in his right foot are surgically fused, and his right heel has suffered one stress fracture.

Yet Warren McCollom gets around.

Many days the 62-year-old retiree drives to Wings and Rice, an East Tucson, Arizona, restaurant, a short distance from his home, and sips Diet Coke as he acts as an informal, and unpaid, host to its clientele. He does this because he likes the restaurant and staff, and the food is good, he says. But life was not always that simple. McCollom is a former United

States Air Force sergeant, who spent his service hitch secretly monitoring Soviet signals traffic from inside Turkey. These days, when he wants some excitement, he visits Las Vegas or Laughlin, Nevada, a miniature Vegas, not so much for the gambling — he restricts himself to nickel slot machines — as for the people watching.

“You might see a movie star, or you might see a farmer from Iowa walking by in his bib overalls,” McCollom says. “One time a guy sat down next to me, a British guy, I guess, and his wife was shopping, so we started talking. He said, ‘This town is amazing. It’s like Disneyland with sin.’”

Sometimes, via the words of Tom Clancy and David Baldacci, McCollom will journey to the bottom of the Atlantic Ocean for secret rendezvous with Soviet submarines or spy upon the efforts of the US Secret Service agents as they battle terrorists.

“The brain is the important part,” he says. “If you don’t keep it moving, the body will just go away. The brain is life. Even if the body does quit on you, so long as you can still think and function, you can live.”

For 37 years, McCollom’s intellectual activity has helped him battle the cause of many of his ailments, Gaucher disease. The National Institute of Neurological Disorders and Stroke defines *Gaucher disease* as an inherited metabolic disorder in which harmful quantities of a fatty substance called glucocerebroside accumulate in the spleen, liver, lungs, bone marrow, and sometimes in the brain.¹ Anemia, fatigue, easy bruising and bleeding, osteoporosis, easily broken bones, and swollen internal organs are among its symptoms.² The carrier rate for the mutations that cause Gaucher disease may be as high as 1 in 15 Jewish people of Eastern European ancestry, and 1 in 100 of the general population, according to statistics compiled by the National Gaucher Foundation.³

McCollom was 26 when he was diagnosed with Gaucher disease type 1, the illness’ most common form. Until then, he says, he enjoyed relatively normal health, with only a few things that, in hindsight, could have been manifestations of Gaucher disease: aches in his legs during his high school years that doctors called growing pains; a liver problem during his college years that was diagnosed as post-viral syndrome; and in his time in the Air Force, an enlarged spleen, fever, and anemia that were called mononucleosis. In 1974, while McCollom was living in rural Illinois, doctors examining him for abdominal pain found an enlarged spleen, and they then assembled a bleak picture from the disparate pieces of McCollom’s puzzling health history.

“Basically, they said, ‘You have this disease. You will maybe live 20 years. We are just treating symptoms because there is no treatment, there is no cure, so enjoy life while you can,’” McCollom recalls.

By 1991, the disease had already caused the painful degeneration of his hips, and McCollom had already endured hip replacement surgery, when he came upon the earliest version of a treatment that he believes has greatly improved his doctors’ predictions: enzyme replacement therapy.

“The brain is life. Even if the body does quit on you, so long as you can still think and function, you can live.”

After almost 2 years taking its predecessor, McCollom started taking twice-a-month, intravenous injections of Cerezyme® (imiglucerase for injection), a modified form of the human enzyme glucocerebrosidase. It's a genetically engineered substance that helps the body break down glucocerebroside.⁴ Blood tests and magnetic resonance imaging revealed that his glucocerebrosidase deposits were decreasing, and his bone density was increasing. “It helped stop my bones from dying. It has increased my platelets, and decreased the anemia and the fatigue. I thought it had stopped my bones from falling apart. My dose was subsequently lowered for almost 2 years, and I later suffered a spinal collapse and knee and foot problems,” McCollom says.

“You get depressed during those things. They're unexpected. They almost blindsides you. You think you are doing fine, and then something like that happens,” McCollom says.

Yet his friends at Wings and Rice say that aside from a limp and some occasional skin discoloration, they see few signs of disease in McCollom today.

“He is just a nice guy. It's always pleasant to see him. He likes helping somebody out. Not just me. If a person gets into something, he always tries to help them out,” says 48-year-old restaurant owner Sung Ho “Ken” Kang. “He's like an extension

of the family, for me. It looks like he takes care of himself pretty well. He's an outgoing person. He likes to talk.”

“He really listens a lot when you talk to him. He is a very understanding person and very helpful too,” said 53-year-old restaurant cashier Rose Torres.

McCollom is philosophical about surviving Gaucher disease and occasionally speaks of his experiences with the ailment at patient meetings and doctors' conferences.

“About 99% of the time, through the whole 37 years of illness, my attitude has been good,” he says. “It's just that there have been these little momentary things that knocked me down, but I got back up. I can't say I went through this big crisis. It just happened. When you have a positive mental attitude, it gets pushed down a little at times, but you never lose it. It's always there.”

References

1. Medline Plus. Gaucher's Disease. Available at: <http://www.nlm.nih.gov/medlineplus/gauchersdisease.html>. Accessed March 11, 2011.
2. National Institute of Neurological Disorders and Stroke. NINDS Gaucher's Disease Information Page. Definition of Disease Symptoms. Available at: http://www.ninds.nih.gov/disorders/gauchers/gauchers.htm#What_is. Accessed March 11, 2011.
3. National Gaucher Foundation Website. Prevalence and Transmission of Gaucher disease. Available at: <http://www.gaucherdisease.org/prevalence.php>. ■

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, thrombocytopenia, bone disease, hepatomegaly, splenomegaly.

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 (enclosed).

Now Recruiting GAUCHER disease ORAL compound clinical research trials

Eliglustat tartrate
(Genz-112638)
is an investigational
oral compound which
aims to partially inhibit
the production of
glucosylceramide
(GL-1) in Gaucher
cells

The ENGAGE and ENCORE studies are designed to determine the safety and efficacy of eliglustat tartrate (Genz-112638) in patients with Gaucher disease type 1.

The **ENGAGE** study is recruiting patients at least 16 years of age with splenomegaly and anemia and/or thrombocytopenia and who have never been or currently are not being treated for the disease. The **ENCORE** study is recruiting clinically stable patients at least 18 years of age who have been treated with enzyme replacement therapy for at least 3 years. The **EDGE** study is recruiting patients to evaluate maintenance of treatment goals comparing twice daily dosing vs. once daily dosing.

These studies require:

- Patients to have a confirmed diagnosis of Gaucher disease type 1
- Patients to be excluded if they have a clinically significant disease, other than Gaucher disease type 1

To participate or learn more about these studies, contact:

■ www.clinicaltrials.gov search

ENGAGE: NCT00891202 **ENCORE:** NCT00943111 **EDGE:** NCT01074944

■ **Genzyme Medical Information at 1-800-745-4447**
(option 2) or medinfo@genzyme.com

One of the world's leading biotechnology companies, Genzyme is dedicated to making a major positive impact on the lives of people with serious diseases.