POMPE Connections

About enzyme replacement therapy and Myozyme

As a person with Pompe disease, you want to understand as much as possible about the treatment that you may receive. Enzyme replacement therapy (ERT) with Myozyme represents the result of years of scientific research and development. Many healthcare professionals, science experts and patients (through participation in clinical trials) around the world have contributed to the development of this medicine. This handout offers insight into what an enzyme replacement therapy is and how Myozyme works in the human body.

Q What is enzyme replacement therapy?

A Enzyme replacement therapy is a medical treatment that replaces a deficient or absent enzyme.

In the case of Pompe disease, one of the lysosomal enzymes called acid alpha-glucosidase or GAA is deficient or missing. As a result, glycogen builds up within the lysosome in the cell. This is usually seen in muscle tissue in the body, such as cardiac, respiratory, skeletal and smooth muscles (muscles found in blood vessels, the bladder or the gastrointestinal tract).

With ERT, a patient with Pompe disease receives regular amounts of the deficient GAA enzyme using a genetically engineered form of the enzyme. The enzyme therapy is delivered intravenously (through the bloodstream). The enzyme travels to the muscles and breaks down the glycogen that causes damage when it builds up in the cells.

Enzyme replacement therapy is a lifelong treatment that is given at regular intervals (for example, twice a month). The total dose is based on the patient's weight.

ERT's are also available for some other lysosomal storage disorders such as Gaucher disease, Fabry disease, and MPS diseases (I, II & VI).

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Other names for Pompe disease

Acid alpha-glucosidase deficiency, acid maltase deficiency (AMD), glycogen storage disorder (GSD) type II, glycogenosis II, and lysosomal alpha-glucosidase deficiency. In different parts of the world, Pompe may be pronounced *"pom-PAY," "POM-puh,"* or *"pom-PEE."*

Q **What is the process for developing new treatments?**

A The process for developing new treatments for diseases starts in the laboratory where researchers begin to test their theories. This is followed by animal studies and, if these go well, by research studies in humans called *clinical trials*. The purpose of these studies is to gather information about the safety of the therapy and how well it works. It takes many years of strict and careful testing before an experimental treatment is approved for use in humans. To learn more, read the Pompe Connections handout entitled '*Medical Progress in Pompe Disease*.'

Q **When did clinical trials for use of ERT and Myozyme in Pompe disease begin?**

A Clinical trials to study the safety and effectiveness of ERT in Pompe disease began in 1999 with a transgenic product derived from rabbit milk. Genzyme began clinical trials for Myozyme in Pompe patients in 2003. Overall, these trials showed that Myozyme provides great benefit when used in Pompe disease, especially when started early in the course of Pompe disease. The infant patients in those early trials showed major improvements in heart muscle function. A number of patients gained skeletal muscle function as well. Some of the infant patients who started on ERT began to walk independently. Of course, it is important to remember that once muscles are severely damaged, they cannot fully regain function and the effectiveness of the drug varies from person to person.

Q **What is Myozyme?**

A Myozyme is currently the only approved ERT treatment for Pompe disease. Myozyme consists of a white powder that is dissolved into a solution for infusion into the body. Myozyme contains the active substance alglucosidase alfa which consists of the human enzyme acid alpha-glucosidase (GAA). Myozyme can only be obtained with a prescription.

Q **What is Myozyme used for?**

A If you have Pompe disease, then your body has a deficiency of an enzyme called alpha-glucosidase. This enzyme normally breaks down glycogen (a carbohydrate) into glucose. If the enzyme is not present, glycogen builds up in certain tissues, particularly your heart (more common in infants) and muscle tissue (including the diaphragm, the main breathing muscle under the lungs, as well as skeletal muscles). The progressive build-up of glycogen causes a wide range of signs and symptoms, including an enlarged heart, breathing difficulties and muscle weakness. This may cause severe disability and even premature death. Myozyme is an enzyme replacement therapy that replaces the missing or deficient enzyme.

Q **How is Myozyme given to Pompe patients?**

A Myozyme treatment is supervised by a physician with experience in the management of patients with Pompe disease, or other inherited diseases of the same type. This is usually a Geneticist, a Pediatrician or Neuromuscular specialist.

Myozyme is used as an intravenous infusion (into a vein) given once every 2 weeks. The recommended dose is 20mg/kg body weight. Myozyme may be administered to children, adolescents, adults or elderly patients.

Q **How does Myozyme work?**

A Myozyme provides you with the enzyme that you are lacking. Upon being infused into a patient, it travels through the blood stream, across the blood vessel barrier and into an area of the body called interstitial space. The final destination for Myozyme is the microscopic region (or sub-organelle) of a muscle cell called a lysosome. The lysosome is where the glycogen accumulates. Once Myozyme arrives in the lysosome, it takes over the job of the absent natural enzyme alpha-glucosidase. That is, it breaks down the buildup of glycogen into glucose.

Q **How is it produced?**

A Myozyme is produced by recombinant DNA technology using a Chinese Hamster Ovary (CHO) cell line. The CHO cell line has been used to manufacture biopharmaceuticals for over 15 years, with over 1 million patients receiving therapeutics manufactured in CHO cells during the past year alone. It is identical in amino acid sequence to a commonly occurring human form of enzyme acid alpha-glucosidase (GAA). Each lot of Myozyme undergoes an extensive series of quality control tests to confirm consistent quality before being released for distribution. Once the manufacturing process is completed, Myozyme is distributed directly by Genzyme through appropriate channels to each country where a patient is undergoing treatment.

For more information about the manufacturing process for enzyme replacement therapy, please visit www.pompe.com where the manufacturing process is explained in more detail.