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Guidance to the Pompe Community on the Management of Myozyme Supply

Conservation of Global Myozyme Supply to Protect Infants and Children with Pompe Disease

*Guidance prepared by the Myozyme Stakeholders Working Group**

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*Please note that some individuals who participated in the Myozyme Stakeholders Working Group are employees of Genzyme or its subsidiaries and other individuals or their institutions or organizations receive or have received funding from Genzyme or its subsidiaries for research, educational activities, and other purposes.

Background

In July of 2008, Genzyme Corporation issued a notification that the worldwide Myozyme® (alglucosidase alfa) supply would be tight in 2009 until European Commission approval of a larger-scale, 4000 liter (L) production facility in Belgium. Genzyme also stated that receiving approval for Myozyme produced at the 4000 L manufacturing scale in the first half of 2009 would greatly improve its ability to return to normal levels of inventory.

Recognizing the need to responsibly manage through a period of increased risk of insufficient supply and to best support people living with Pompe disease worldwide, the International Pompe Association (IPA) worked with Genzyme to form an international Myozyme Stakeholders Working Group (MSWG) in August, 2008. The group was comprised of members of the IPA, Genzyme, and several physician experts in the management of Pompe disease from the US and Europe. The MSWG met frequently over the course of several months to discuss options for the clinical management of patients who could be affected by a period of intermittent delays in supply. The goal of the MSWG was to develop practical guidance for clinicians and patients.

The MSWG identified infants and children as a particularly vulnerable group who may have the most rapid rate of progression of the disease. This guidance integrates currently available knowledge about the relative risk associated with missing infusions of Myozyme for infants and children, and aims to minimize any disruption of supply in this higher risk population.

Unless appropriate measures are taken, we now recognize that we are entering a period of extremely tight inventory levels for Myozyme where delays in shipments resulting in potential interruptions in therapy may occur. Physicians involved in the treatment of Pompe patients with Myozyme therapy and patients receiving Myozyme therapy are strongly encouraged to follow these recommendations.

Recommendations

Due to an increasingly tight Myozyme supply beginning in January of 2009, the following recommendations should be followed for the treatment of individuals with Pompe disease worldwide. Adherence to these guidelines is necessary to conserve the Myozyme supply for infants and children and to strive to avoid unanticipated interruptions of shipments.

Infants and Children (individuals prior to their 19th birthday[1]):

All infants and children should continue to receive their prescribed treatment without any interruptions, and all newly diagnosed infants and children should start therapy as recommended by their physician.[2] [3]

Adults (individuals who have reached their 19th birthday or older):

No new adult patients should initiate therapy until Myozyme inventory levels return to normal. If there are genuine concerns about not initiating treatment for newly identified, severely affected patients, physicians should contact Genzyme Medical Information.

For every adult who has been receiving Myozyme therapy on a commercial, charitable, or temporary access basis, the following infusion schedule is recommended:

- Adults worldwide should receive monthly infusions beginning in January until Myozyme inventory levels return to normal. This means adults should immediately cancel their infusion between January 15th and January 31st and cancel one infusion each month until further information becomes available from Genzyme.[4]

Worldwide implementation of this modification to treatment schedules beginning in January for adults is essential; this will help ensure that no infant or child will miss an infusion due to potential shipping interruption or delay during this finite period.

The MSWG arrived at these recommendations based on the best available information provided by Genzyme on the Myozyme supply situation. Health care professionals are advised to take this guidance into account when exercising their clinical judgment. Where there are genuine concerns about modifying the treatment schedule of severely affected patients, physicians should contact Genzyme Medical Information.

Rationale and Evidence Supporting Recommendations

1) The United Nations Convention on the rights of the Child indicates the defined age of a child as “any person under the age of 18.” The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use defines an adolescent as 12 to 16-18 years of age dependent on the region. Less than 19 years of age was recommended as an inclusive age cutoff that can be widely accepted world wide.

2) As per the Myozyme prescribing information, the recommended dose is 20mg/kg per infusion. However, if an individual has been prescribed a different dose, then it would be the treating physician’s decision to maintain or change the dose.

3) Infants and children with Pompe disease may have a more rapidly progressive rate of the disease by virtue of their age at presentation and/or the nature of mutations in the alpha-glucosidase gene. Thus, they may be at greater risk of irreversible delay in development and muscle damage. Infants with cardiac involvement are at the highest risk of death. Presentation in childhood carries an additional burden of disease because the growing child is at significant risk of developing irreversible skeletal deformation (scoliosis in particular).

4) Since only a relatively low percentage of administered enzyme ultimately reaches the lysosomes in skeletal muscle tissues, it is believed that a minimum peak level is needed to achieve adequate enzyme levels. Thus, it is recommended to administer the full prescribed dose of Myozyme less frequently (up to 4 weeks) for this short period of time rather than administering a lower dose at the standard frequency of every 2 weeks.