

FOOD AND DRUG ADMINISTRATION (FDA)
CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)
Endocrinologic and Metabolic Drugs Advisory Committee Meeting
October 21, 2008

The committee will discuss the safety and efficacy of biologic license application (BLA) 125291, MYOZYME (alglucosidase alfa), Genzyme Corp., for the treatment of late onset Pompe disease.

Errata for Open Session Alglucosidase Alfa 2000L product

1. Page 8, 3rd paragraph: Change “All patients with GAA activity < 1% developed inhibitory antibodies to 2000 L product, and this group demonstrated no improvement in either 6MWT or % predicted FVC at the last observation (see section 5.4.5).” to “One of six patients with GAA activity < 1% developed inhibitory antibodies to 2000 L product. This group of patients with GAA activity <1% demonstrated no improvement in either 6MWT or % predicted FVC at the last observation (see section 5.4.5)”
2. Page 47, 2nd paragraph: Remove sentence “However, all six of the patients with GAA activity < 1% (Patients 16708, 18701, 65706, 65707, 90709, and 90710) who received 2000 L product developed inhibitory antibodies to 2000 L product.”
3. Page 47, 3rd paragraph: Change “Overall, these observations regarding patients with GAA activity <1% are concerning for a population of patients that are younger, may have more severe disease at baseline, may not respond as well to treatment with 2000 L product, and may be at risk for more significant immune responses to the 2000 L product.” to “Overall, these observations regarding patients with GAA activity <1% are concerning for a population of patients that are younger, and may have more severe disease at baseline.”
4. Page 68, last paragraph: Change “Additionally, patients with GAA activity level <1% all developed inhibitory antibody to 2000 L product, and the treatment effect in these patients (n=6) was reduced.” to “Additionally, patients with GAA activity level <1% demonstrated a reduced the treatment effect (n=6).”
5. Page 9, 2nd paragraph: Change last sentence from “Immunogenicity of the 2000 L product is concerning, as 100% of 2000 L-treated patients developed anti-rhGAA IgG antibodies, and all patients with GAA activity <1% developed inhibitory antibodies.” to “Immunogenicity of the 2000 L product is concerning, as 100% of 2000 L-treated patients developed anti-rhGAA IgG antibodies, and 30% of patients developed inhibitory antibodies to GAA.”
6. Page 60, first paragraph: after first sentence ending “. . . (i.e., possibly, probably, or definitely related).” Insert “AEs that occurred after the observation period could also be considered IARs at the discretion of the investigator.”

FOOD AND DRUG ADMINISTRATION (FDA)
CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)
Endocrinologic and Metabolic Drugs Advisory Committee Meeting
October 21, 2008

The committee will discuss the safety and efficacy of biologic license application (BLA) 125291, MYOZYME (alglucosidase alfa), Genzyme Corp., for the treatment of late onset Pompe disease.

7. Page 9, last paragraph: change first sentence from “Chronic exposure to 160 L product has led to the development of immune mediated adverse events including skin rashes and at least one report of immune-mediated glomerulonephritis.” to “Chronic exposure to 160 L product has led to the development of immune mediated adverse events including skin rashes. Use of Pompase™ (an earlier form of enzyme replacement therapy for Pompe disease) has been associated with at least one report of immune-mediated glomerulonephritis.”
8. Page 65, first paragraph: change first sentence from “There has been at least one report in the literature of the development of membranous glomerulonephritis associated with treatment with the 160 L product.” to “There has been at least one report in the literature of the development of membranous glomerulonephritis associated with treatment with Pompase.”
9. Page 65, first paragraph: Change third sentence from “Patient 29705” to “Patient 29708”
10. Page 14, paragraph 1, second sentence: “The Agency also had concerns that due to manufacturing differences for the two products, the 2000 L product may be less potent than the 160 L product, although this could not be definitively established given the limitations of the data.”

Change to: The Agency also had concerns that due to manufacturing differences for the two products, the 2000 L product may have a lesser biological effect than the 160 L product, although this could not be definitively established given the limitations of the data.

11. Page 38, paragraph 2, last sentence: “Thus, given the concerns regarding the potency of 2000 L product compared with 160 L product, the potential for increased immunogenicity of 2000 L product (see section 7.4.5), and the lack of data regarding efficacy of 2000 L product in the juvenile-onset patients, strong consideration should be given to limiting the indication of 2000 L product to adult-onset patients only.”

Change to: Thus, given the concerns regarding the potential for increased immunogenicity of 2000 L product (see section 7.4.5), and the lack of data regarding efficacy of 2000 L product in the juvenile-onset patients, strong consideration should be given to limiting the indication of 2000 L product to adult-onset patients only.

FOOD AND DRUG ADMINISTRATION (FDA)
CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)
Endocrinologic and Metabolic Drugs Advisory Committee Meeting
October 21, 2008

The committee will discuss the safety and efficacy of biologic license application (BLA) 125291, MYOZYME (alglucosidase alfa), Genzyme Corp., for the treatment of late onset Pompe disease.

12. Page 51, last paragraph, last sentence: “Thus, given the concerns regarding the potency of 2000 L product compared with 160 L product, the potential for increased immunogenicity of 2000 L product (see section 7.4.5), and the lack of data regarding efficacy of 2000 L product in the juvenile-onset patients, strong consideration should be given to limiting the indication of 2000 L product to adult-onset patients only.”

Change to: Thus, given the concerns regarding the potential for increased immunogenicity of 2000 L product (see section 7.4.5), and the lack of data regarding efficacy of 2000 L product in the juvenile-onset patients, strong consideration should be given to limiting the indication of 2000 L product to adult-onset patients only.

13. Page 68, paragraph 2, last sentence: “Thus, given the concerns regarding the potency of 2000 L product compared with 160 L product, the potential for increased immunogenicity of 2000 L product (see section 7.4.5), and the lack of data regarding efficacy of 2000 L product in the juvenile-onset patients, strong consideration should be given to limiting the indication of 2000 L product to adult-onset patients only.”

Change to: Thus, given the concerns regarding the potential for increased immunogenicity of 2000 L product (see section 7.4.5), and the lack of data regarding efficacy of 2000 L product in the juvenile-onset patients, strong consideration should be given to limiting the indication of 2000 L product to adult-onset patients only.